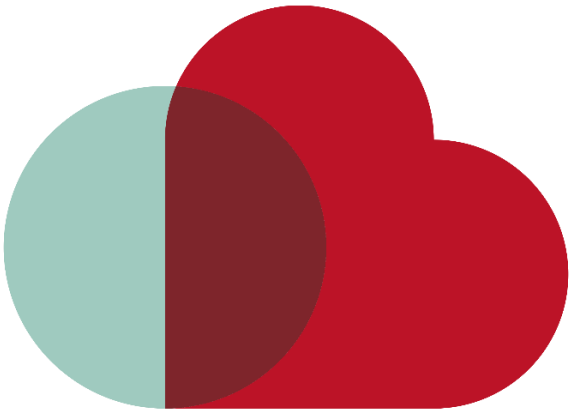

retention
SMART HEART FAILURE MANAGEMENT

Horizon 2020 Project RETENTION

"HEART FAILURE PATIENT MANAGEMENT AND INTERVENTIONS USING CONTINUOUS PATIENT MONITORING OUTSIDE HOSPITALS AND REAL WORLD DATA"

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** The project uses a multi-stage internal review and release process, with defined milestones. Milestone names include abbreviations/terms as follows:*

TOC = "Table of Contents" (describes planned contents of different sections);

- *Intermediate: Document is approximately 50% complete – review checkpoint;*

ER = "External Release" (i.e. to commission and reviewers);

- *Proposed: document authors submit for internal review;*
- *Revised: document authors produce new version in response to internal reviewer comments approved: Internal project reviewers accept the document.*

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Executive Summary

Deliverable D3.1 entitled “RETENTION Requirements’’ is the first deliverable of “WP3 – RETENTION Clinical and System Requirements & Platform Design”. The deliverable presents the results of the user requirement elicitation process performed from M01 to M06 of the RETENTION project within the activities of Tasks 3.1 & 3.2. More specifically, a state of-the-of art analysis for Heart Failure patient telemonitoring was conducted including numerous studies evaluating remote patient monitoring with invasive and non-invasive parameters, the current trends in technology solutions regarding Artificial Intelligence and Decision Support in HF, Smart home and IoT devices in healthcare, Real World Data in Healthcare, Big Data Management and analytics, Human-Computer Interactions, Security, Privacy and Trust in healthcare and IoT systems and Systems and Applications. Also, it was included the current clinical practice used and the regulations and policies point of view. Several EU, national and international R&D projects and initiatives relevant to RETENTION project were documented. The Clinical study characteristics were outlined, including inclusion and exclusion criteria for the three different types of patients: HF patients, VAD patients, Heart Transplant recipients and a detailed list of variables based on clinical practice and state-of-art research that should be monitored, the frequency when they will be monitored, and other provided functionalities. The variables were assigned with high, medium, low priority depending on the strong (or not) evidence that can be associated with patient status.

The RETENTION ecosystem was also defined with the users (patients, caregivers, clinicians), the secondary users (public health experts, data scientists/researchers, hospital IT) and the stakeholders (hospitals, researchers, biomedical industry) of the platform. Based on that, a user requirement elicitation process was established by the relevant partners and the collected information was the basis for the preparation of specific questionnaires and interviews, targeting in user needs identification. In total, 163 questionnaires were obtained from the 5 participant hospitals. Specifically, the consortium partners provided 74 questionnaires for patients, 55 questionnaires for caregivers and 34 for clinicians. To be aware of the potential technical barriers in the implementation of the RETENTION platform, an interview with the responsible person of the IT department in each of the 5 participant hospitals was performed. The results of the questionnaires and interviews were used for defining the user requirements. The requirements were collected in terms of functionalities, usability, performance, availability and reliability, legal and ethical, security and privacy, data and data exchange and scalability. Those requirements are translated into non-functional and functional requirements of the RETENTION platform. Based on the user requirements, a range of different use cases and scenarios are described in detail for clinicians, patients and users.

1 About this document

Over recent years, there has been an increase in interest in e-health monitoring systems, leading to the creation of Health Smart Homes. Such technologies can facilitate the monitoring of patients' activities and enable healthcare services at home. They improve the quality of elder population well-being in a non-obtrusive way, allowing greater independence, maintaining good health, preventing social isolation for individuals and delay their placement in institutions such as nursing homes and hospitals. Their development was enabled by major advances in wireless technology and computing power, leading to an increasing number of connected medical devices that can generate, collect, analyse, and transmit data. The data, along with the devices themselves, are creating the Internet of Medical Things (IoMT) – a connected infrastructure of medical devices, software applications and health systems and services. The IoMT is rapidly transforming healthcare delivery. More specifically, connectivity between sensors and devices is enabling health care organisations to streamline their clinical operations and workflow management, and improve older adults care, even from remote locations, such as their home.

The overarching concept of RETENTION is to integrate heterogeneous smart consumer and medical devices, to enable the continuous collection of data from the everyday life of the Heart Failure (HF) patient, which will be analysed to obtain the evidence needed to offer personalised interventions to promote their healthy and independent living. RETENTION will leverage (big) data analytics and learning capabilities, allowing for large-scale analysis of the abovementioned collected data, to generate the evidence required for making decisions about personalised interventions. Privacy-preserving and secure by design data handling capabilities, covering data at rest, in processing, and in transit, will cover comprehensively the RETENTION platform.

The aim of RETENTION is to develop and deliver an innovative platform supporting enhanced clinical monitoring and interventions aimed at improving the clinical management of patients with chronic heart failure (HF), left ventricular assist devices (LVAD) or heart transplant (HT) carriers reducing their mortality and hospitalization rates, and improving their quality of life, safety, and well-being.

The RETENTION platform will support clinical decision making and evidenced based personalized interventions for HF patients by: (a) continually monitoring and collecting medical, clinical, physiological, behavioural, psychosocial, and real-world data for such patients, (b) analysing these data using innovative model-driven big data analytics, statistical, artificial intelligence and machine learning techniques, (c) detecting patterns in the HF disease progression and the quality of life of patients, (d) cross checking and validating them against the clinical literature, and (e) offering transparent, explainable and verifiable decision making capabilities that leverage the evidence produced by the underlying data analysis and augment clinical studies targeting HF and other cardiovascular diseases.

1.1 Role of deliverable

This document corresponds to "D3.1 RETENTION Requirements'', the first deliverable of "WP3 - RETENTION Clinical and System Requirements & Platform Design". This deliverable describes the work that has been performed for definition of the requirements of the RETENTION solution, covering patients' clinical

management, user, and platform requirements. The role of the document is to define the requirements needed for the design of the RETENTION Platform.

In this document RETENTION requirements are defined from the perspective of managing the health and well-being of patients suffering from HF: slowing the progression of the disease, and improving their quality of life, safety, and well-being. Moreover, aspects such as promoting active (physically and cognitively) living, healthy habits, and providing conditions that facilitate safe and healthy living of the patients are also considered.

A patient centric design methodology has been followed. Surveys and interviews have been carried out, making sure that all needs across the spectrum of HF patients have been covered. These groups have also included informal caregivers (i.e., family members of HF patients) making sure that their needs are also addressed. We have also included clinicians, technical personnel's opinion to design the platform.

This document also focuses on defining the platform functional and non-functional requirements from technical perspective (e.g., interfacing capabilities, supported interactions, compute and networking capabilities), conducting an up-to-date analysis of the pertinent technological landscape and the identification, specification, and prioritization of system requirements for it. Finally, this task also specifies the security & privacy, as well as continuous assurance requirements, considering the regulatory landscape in each of the participating countries and the EU.

This document is the basis of for Deliverable D3.2 (RETENTION Platform Architecture & Design), which will focus on specifying the initial reference architecture for the RETENTION platform and the digital services that it will offer.

1.2 Relationship to other RETENTION deliverables

This deliverable is closely related to:
- D3.2: RETENTION architecture as it sets the base of the RETENTION platform
- D8.2 RETENTION Clinical trial protocol and evaluation framework as variables to be monitored are selected.

1.3 Structure of the document

The current deliverable provides the requirements of the RETENTION system. Specifically it aims to define the requirements collected from different end users and are related to the management of HF patients and also the system requirements from a technical point of view, following a specific patient-centric design methodology. The deliverable includes 8 sections and the Appendix. Thus, the structure of the D3.2 is as follows:

Section 1 presents the purpose, scope, structure of this deliverable and the relation to the Description of Action (DoA).
Section 2 presents the current state of the art of Heart Failure patient monitoring from clinical and technological perspective
Section 3 addresses the user requirements that resulted from the dedicated questionnaires and interviews that prepared from both clinical and technical partners.
Section 4 addresses the clinical characteristics, variables to monitor
Section 5 describes different use case scenarios based on the analysis of the collected user requirements
Section 6 presents the functional and non-functional requirements in tabular form.
Section 7 and 8 refer to conclusions, references, and the Appendix section, that includes the questionnaires, interviews.

Table 1. Relation with the RETENTION DoA

DoA Task Description	Addressed by D3.1
T3.1: This task will define the requirements of RETENTION from the perspective of the managing the health and well-being of patients suffering from HF. These will cover requirements related to the management of patients with HF and patient response to it, slowing the progression of these diseases, and improving the quality of life, safety, and well-being of the patients. Moreover, aspects such as promoting active (physically and cognitively) living, healthy habits, and providing conditions that facilitate safe and healthy living of the patients will be considered. A patient centric design methodology will be followed with frequent user focus groups from day one of the project making sure that all needs across the spectrum of HF patients will be covered. These groups will also include informal carers (i.e. family members of HF patients) making sure that their needs are also addressed. *T3.2: This task will focus on defining the platform requirements from technical perspective (e.g. interfacing capabilities, supported interactions, compute and networking capabilities), conducting an up-to-date analysis of the pertinent technological landscape (based on the State of the Art presented in Section 1.4.1), and the identification, specification and prioritisation of system requirements for it. It will also define an initial list of user-related requirements, such as user interfacing, visualization, and intervention delivery preferences, which will be further refined during the development of the associated components in WP5. Finally, this task will also specify the security & privacy, as well as continuous assurance requirements, considering the regulatory landscape in each of the participating countries and the EU as a whole.*	This deliverable defines the requirements of the RETENTION system, as they are described in both Tasks 3.1 & 3.2. More specifically, D3.1 presents the clinical and technical requirements as resulted from the provided questionnaires and interviews answered by the RETENTION users by following a specific user requirements elicitation methodology (section 3). Following this, the participating partners built different use case scenarios for each user role (clinicians, patients, carers) (section 5). An up-to-date analysis of the current State of the Art in Heart failure patient monitoring was also conducted highlighting the current clinical practice, the technology related solutions and the policies (and policies' needs) for HF in Europe (section 2). In addition, the functional and non-functional requirements that emerged from questionnaires and focus groups were addressed (section 6). The deliverable also presents the clinical study characteristics including the inclusion and exclusion criteria, the variables that will be monitored throughout the project lifecycle and the proposed RETENTION technology solutions (section 4).

2 Remote patient monitoring in heart failure: Clinical practice and state of the art technology solutions

2.1 Heart failure: definition and epidemiology

Heart failure (HF) is a clinical syndrome characterized by the inability of the heart to deliver adequate cardiac output and resulting in typical symptoms (e.g., breathlessness, ankle swelling and fatigue) that may be accompanied by signs (e.g., elevated jugular venous pressure, pulmonary crackles, and peripheral oedema). The syndrome is caused by a structural and/or functional cardiac abnormality, in which the reduced cardiac output is often associated with elevated intracardiac pressures at rest or during stress (2).

Currently the incidence of HF in Europe is about 3/1000 person-years (all age-groups) or about 5/1000 person-years in adults. The prevalence of HF in Europe is 1-2% of adults (1–3) and it increases with age: from around 1% for those aged <55 years to >10% in those aged 70 years or over (4). It is also estimated that more than 50% of HF patients are women(5).

HF is a heavy burden on health systems due to the multiple, prolonged hospitalizations and the related management costs. Each hospitalization has been shown to decrease the patient's life expectancy and quality of life. Due to population growth, ageing, and the increasing prevalence of comorbidities, the absolute number of hospital admissions for HF is expected to increase considerably in the future, perhaps by as much as 50% in the next 25 years (6). As a result, remote patient monitoring has emerged as a promising tool for predicting upcoming decompensation episodes and improving patient's survival and quality of life.

Recently, a new European Society of Cardiology (ESC) HF guidelines has been published (7). In this document, ESC recognised that non-invasive telemonitoring could be useful for HF patients, but more evidence is needed.

In the last stages of HF, some selected patients can be candidates to HT or an LVAD. These therapeutic options have demonstrated to increase survival, but at expenses of an intensive follow-up and repeated hospitalizations.

The aim of RETENTION system is to develop and deliver an innovative Artificial Intelligence (AI)-enabled platform supporting enhanced clinical monitoring and interventions aimed at improving the clinical management of patients with chronic HF, HT or LVAD carriers.

2.2 Current clinical practice in heart failure monitoring and management

The European Society of Cardiology on Heart Failure Guidelines recommend telemonitoring with a class IIB, that means that telemonitoring may be consider. The level of evidence is B; it means that data is derived from a single randomized clinical trial or large non-randomized studies. In clinical practice, telemonitoring is not implemented as a usual clinical practice in most of the European cardiology services.

European Society of Cardiology recommendations (8) focus on an early visit in patients recently admitted for acute HF to prevent readmissions in the most vulnerable phase. However, despite this early visit no other recommendations are made, and follow-up of patients are widely variable between countries and centres. In academic centres with high volume, there are usually specialized HF units with trained doctors and nurses that assume this early visit. According to the patient status and the need of HF drugs up titration among others, a visit schedule is proposed with visits approximately every 2 weeks. Follow-up in those specialized

units is also variable but is common to derive the patient again to his/her general cardiologist or primary care 6 months after discharge whenever the patient is stable (9).

After a thorough literature review, the remote monitoring approach can be divided into two types: Non-invasive (weight, heart rate, ECG, blood pressure, symptoms…) and invasive parameters (thoracic impedance, haemodynamic, etc.). In the following subsections the two different types of parameters are presented in detail.

The focus will be mainly on heart failure patients, since telemonitoring systems in heart transplantation patients and VAD patients are scarce and there are not important randomized clinical trials on these populations.

2.2.1. Non-invasive parameters (weight, heart rate, ECG, blood pressure and symptoms).

Numerous studies evaluating remote patient monitoring with simple parameters (weight, heart rate, ECG, blood pressure and symptoms) have been performed in the last 10 years. Although there are some large studies, most of them have been single-centre cohorts evaluating heterogeneous patient populations.

In 2010, Chaudhry et al. (10) published the Tele-HF trial. A total of 1,653 HF patients were randomised to telemonitoring performed by phone calls or usual care. During each call, patients heard a series of questions about general health and HF symptoms, and they responded using the telephone keypad. Clinicians received the information and acted in consequence. The study did not find significant differences between the two groups in terms of cardiovascular mortality, hospitalizations, or number of days in hospital.

In 2016, the BEAT-HF trial (11) was published. It was a multicentre randomised trial which compared a telehealth-based care transition intervention vs usual care for older patients who were discharged after a decompensated HF episode. The intervention was composed by: predischarge HF education, regularly scheduled telephone coaching, and home telemonitoring of weight, blood pressure, heart rate, and symptoms. In this study, remote patient monitoring did not reduce mortality or hospitalizations during the first 180 days after discharge, but improved quality of life.

In 2018, the TIM-HF2 trial (12) was published. In this multicentre trial 1,571 HF patients were randomly assigned to remote patient management or usual care. The remote patient monitoring consisted of daily transmission of body weight, systolic and diastolic blood pressure, heart rate, analysis of the heart rhythm, peripheral capillary oxygen saturation (SpO2) and a self-rated health status (scale range one to five) to the telemedical centre. Patient telemonitoring system was composed by a three channels electrocardiogram, a blood pressure device, weight scales, a saturometer and a mobile phone. Telemonitoring data was combined with blood analysis/test to create a patient risk profile. In this trial, remote patient management group presented a reduction in days lost due to unplanned cardiovascular hospital admissions and all-cause death (hazard ratio 0.80, 95% CI 0.65–1.00; p=0.046).

In 2018, Yun et al. (13) published a meta-analysis of 37 randomized clinical trials including 9,582 patients between 2001-2016 aimed to evaluate the effectiveness of telemonitoring in the management of patients with HF. Most of these studies evaluated heart rate, blood pressure and weight. In this meta-analysis, the risks of all-cause mortality (risk ratio [RR] 0.81, 95% confidence interval [CI] 0.70–0.94) and HF-related mortality (RR 0.68, 95% CI 0.50–0.91) were significantly lower in the telemonitoring group than in the usual care group. Remote monitoring showed more benefit when ≥3 biologic data were transmitted or when transmission occurred daily. Telemonitoring also reduced mortality in the studies that patients' symptoms, medication adherence, or prescription changes were monitored. However, all-cause hospitalizations and HF-related hospitalizations were not reduced.

Study	Country	No. of Patients (TM/UC)	Mean Age, y	Male, %	NYHA	Biologic Information	TM Characteristic	Transmission Frequency	Follow-Up
Ong 2016[21]	USA	715/722	73	53.8	I–IV	Weight, BP, pulse	Asynchronous	Daily	6 mo
Bekelman 2015[10]	USA	187/197	68	96.6	I–IV	Weight, BP, pulse	Asynchronous	Daily	12 mo
Idris 2015[17]	USA	14/14	58.5	39.5	II/III	Weight, BP, heart rate, oxygen saturation	Asynchronous	Daily	3 mo
Pedone 2015[22]	Italy	47/43	79.7	38.5	II–IV	Weight, BP, heart rate, oxygen saturation	Asynchronous	Daily	6 mo
Blum 2014[32]	USA	104/102	72.5	71.4	II–IV	Weight, BP, heart rate, ECG	Asynchronous	Daily	4 y
Villani 2014[29]	Italy	40/40	72	73.7	III/IV	Weight, pulse, BP, ECG	Asynchronous	Various, eg, weight daily, ECG weekly	12 mo
Vuorinen 2014[30]	Finland	47/47	58	83	II–IV	Weight, BP	Asynchronous	Weekly	6mo
Krum 2013[28]	Australia	188/217	73	63	II–IV	Weight	Asynchronous	Monthly	12 mo
Madigan 2013[39]	USA	54/45	74.9	32.3	II–IV	Weight, BP, pulse, oxygen saturation	Asynchronous	Daily	6 mo
Dendale 2012[15]	Belgium	80/80	76	65	I–IV	Weight, BP, heart rate	Asynchronous	Daily	6 mo
Pekmezaris 2012[35]	USA	83/85	82	38.1	I–IV	BP, pulse	Synchronous	NR	3 mo
Seto 2012[23]	Canada	50/50	53.7	79	I–IV	Weight, BP, ECG	Asynchronous	Daily	6 mo
Bowles 2011[11]	USA	101/116	72.4	34.6	NR	Weight, BP	Combined	Daily	6 mo
Koehler 2011[19]	Australia	354/356	66.9	81.3	II/III	Weight, BP, ECG	Asynchronous	Daily	12 mo
Antonicelli 2010[40]	Australia	29/28	78.2	57.9	II–IV	Weight, BP, heart rate, ECG, 24-h urine	Asynchronous	Daily	12 mo
Chaudhry 2010[13]	USA	826/827	61	57.9	I–IV	Weight	Asynchronous	Daily	6 mo
Kulshreshtha 2010[20]	USA	82/68	67.6	63.3	NR	Weight, BP, heart rate, oxygen saturation	Asynchronous	Daily	6 mo
Weintraub 2010[25]	USA	95/93	69	65.9	I–IV	Weight, BP, heart rate	Asynchronous	Daily	3 mo
Dar 2009[33]	UK	91/91	71	66.4	II–IV	BP, heart rate, oxygen saturation	Asynchronous	Daily	6 mo
Giordano 2009[27]	Australia	230/230	57	85.2	II–IV	Weight, BP, ECG	Synchronous	Every week or every 15 days	12 mo
Mortara 2009[34]	Italy	94/101/106/160	60	84.5	II–IV	Weight, BP, heart rate, etc	Asynchronous	Others (eg, weight, BP: weekly, ECG: daily)	12 mo
Scherr 2009[38]	Austria	54/54	66	70.8	II–IV	Weight, BP, heart rate	Asynchronous	Daily	6 mo
Wakefield 2009[41]	USA	52/47/49	69.3	99	II–IV	Weight gain	Synchronous	Weekly	12 mo
Antonicelli 2008[8]	Australia	28/29	78.2	57.9	II–IV	Weight, BP, heart rate, ECG	Asynchronous	Daily	12 mo
Balk 2008[9]	Netherlands	101/113	66	70.1	I–IV	Weight, BP	Asynchronous	Daily	Mean 288 d
Dansky 2008[37]	USA	127/45/12	77	NR	NR	Weight, BP, pulse	Combined	Daily	4 mo
Kashem 2008[18]	USA	24/24	53.5	74	II–IV	Weight, BP, heart rate	Asynchronous	NR	12 mo
Schwarz 2008[42]	USA	51/51	78.1	48	II–IV	Weight	Asynchronous	Daily	3 mo
Soran 2008[24]	USA	160/155	76	34.9	II/III	Weight	Asynchronous	Daily	6 mo
Wakefield 2008[31]	USA	52/47/49	69.3	99	II–IV	Weight, BP	Synchronous	Weekly	12 mo
Woodend 2008[43]	Canada	62/59	66	75	II–IV	Weight, BP, ECG	Combined	Daily	12 mo
Kashem 2006[36]	USA	18/18	56.1	66.7	II–IV	Weight, BP, heart rate	Asynchronous	Daily	8 mo
Cleland 2005[14]	Netherlands	173/168/85	67.3	77.2	I–IV	Weight, BP, pulse, ECG	Asynchronous	Daily	450 d
Capomolla 2004[12]	Italy	67/66	57	87.9	II–IV	Weight, systolic BP, heart rate, etc	Asynchronous	Daily	12 mo
Goldberg 2003[16]	USA	138/142	59	67.5	III/IV	Weight	Asynchronous	Daily	6 mo
Jerant 2003[44]	USA	13/12/12	70.3	45.9	II–IV	Vital signs	Synchronous	Daily	6 mo
de Lusignan 2001[26]	UK	10/10	75.2	NR	NR	Vital signs	Combined	NR	12 mo

BP, blood pressure; ECG, electrocardiography; NR, not reported; NYHA, New York Heart Association functional class; TM, telemonitoring; UC, usual care.

Figure 1. Studies included in the Meta-analysis (Yun et al. Comparative effectiveness of Telemonitoring versus usual care for Heart Failure).

There is some evidence that other parameters like temperature, air humidity and pollution can affect to HF, LVAD and HT patients (14–18). However, there are no large-scale studies on effects of monitoring those real-world data.

2.2.2 Invasive parameters

-Related to cardiac implantable electronic devices (CIED) (pacemakers/cardiac resynchronization therapy / implantable cardiac defibrillator): This section includes, the remote monitoring of CIED functions and remote monitoring of other parameters related with HF decompensations (thoracic impedance, heart rate, respiratory rate…).

- **Remote monitoring of CIED functions:** In 2010, the TRUST trial (19) showed the safety of CIED home monitoring. Moreover, home monitoring detected generator and lead problems earlier than conventional care and reduced the need of in-hospital device evaluation (20). Since then, CIED home monitoring have become a usual practice in many centres.
  CIEDs can detect different types of atrial and ventricular arrhythmias through one or more intracavitary catheters. Auricular catheter can detect auricular high-rate episodes (AHRE) in patients without history of atrial fibrillation (AF). AHRE are related to occurrence of HF, progression to AF and stroke (21–23). An early detection of patients with a high frequency or AHRE could improve outcomes in HF patients. Nowadays, the main clinical application of remote monitoring of CIEDs is the promptly identification of asymptomatic episodes of AF, flutter and ventricular tachycardias.

- **Remote monitoring of other parameters related with HF decompensations**: Many commercially available CIEDs allows the measurement of intrathoracic impedance, which is inversely correlated with pulmonary capillary wedge pressure and fluid balance. Intrathoracic impedance was one of the first parameters introduced in CIED to monitor HF patients. After intrathoracic impedance other variables have been used to monitor HF patients such as heart rate variability, AF burden, respiratory rate, or patient´s physical activity. Several studies revealed that a combination of these parameters could predict HF hospitalizations (24–26).
  However, the clinical benefit of CIED telemonitoring in HF patients is controversial. IN-TIME (27) is the only trial that showed a clinical benefit of CIED telemonitoring in HF patients. A total of 664 patients were randomized to telemonitoring of CIED vs standard care. The parameters measured by the CIED were ventricular and atrial tachyarrhythmia episodes, low percentage of biventricular pacing, increase in the frequency of ventricular extrasystoles, decreased patient activity, and abnormal intracardiac electrogram. A composited score of HF (all-cause death, overnight hospital admission for HF, change in NYHA class, and change in patient global self-assessment) was evaluated. The trial showed that telemonitoring improved the composite score in compared to usual care, although no differences in HF hospitalizations or mortality were observed. Other studies have not showed a clinical benefit in CIED telemonitoring (28,29). In 2020, Alotaibi et al. (30)published a meta-analysis of 13 studies of implantable cardiac devices to telemonitoring HF patients. This analysis included also other invasive hemodynamic monitoring systems and not only CIEDs-based telemonitoring studies. In the CIEDs-based telemonitoring studies analysis no differences were found between groups.

Authors	Device	Measured parameters	Funding	Countries	Centres
Abraham	ICD with or without CRT. Implantable continuous hemodynamic monitor	PA pressure	St Jude	USA	Multicentre
Adamson	ICD and implantable continuous hemodynamic monitoring device.	RV pressure	Medtronic	USA	Multicentre
Al-Khatib	ICD with or without CRT Medtronic CareLink	Arrhythmias.	Medtronic	USA	Single
Boriani	CRT-D and ICD Carelink monitor and automatic alerts for lung fluid accumulation (OptiVol®)	Lung imped-ance	Medtronic	8 European countries and Israel	Multicentre
Bourge	ICD with or without CRT. Implantable continuous hemodynamic monitor	RV pressure	Medtronic	USA	Multicentre
Domenichini	ICD with or without CRT CRT-D device equipped with Medtronic OptiVol or SJM CorVueTM	Lung imped-ance	Medtronic, St Jude, Cardiovascular Biomedical Research Unit, Barts Health NHS Trust	UK	Single
Hansen	ICDs with or without CRT CRT-Ds Merlin@home trans-mitter	Arrhythmias	Abbott	Germany	Multicentre
Hindricks	Dual chamber ICD or CRT-D Biotronik Home Monitoring function	Arrhythmias.	Biotronik	Australia, Europe, Israel	Multicentre
Landolina	ICD or CRT-D. OptiVol Medtronic	Lung imped-ance	Italian ministry of health and Medtronic	Italy	Multicentre
Luthjel	ICD with or without CRT Medtronic CareLink network. OptiVol	Lung imped-ance	Medtronic	Germany	Single
Morgan	ICD, CRT from three manufacturers: Medtronic, Boston, St Jude	Lung imped-ance. Heart rate variabili-ty.	British Heart Foundation and Medtronic	UK	Multicentre
van Veldhuis-en	ICD alone or CRT, including intrathoracic impedance (OptiVol) and cardiac compass trends	Lung imped-ance	Medtronic	Europe (most patients), Africa, Middle East and Asia	Multicentre
Varma	ICD	Arrhythmias	Biotronik	USA	Multicentre

ICD, intracardiac defibrillator; CRT, cardiac resynchronisation therapy; PA, pulmonary artery; RV, right ventricle

Figure 2. Studies included in the Meta-analysis performed by Alotaibi et al. Obtained from Alotaibi et al., «Remote Monitoring of Implantable Cardiac Devices in Heart Failure Patients».

-Invasive hemodynamic monitoring devices: Several devices have been tested to perform an invasive hemodynamic telemonitoring (31). However, only CardioMEMS have showed a clinical benefit. CardioMEMS is a micro pressure transducer which is implanted in a left posterior pulmonary artery for daily measurements

of pulmonary artery pressures. The CHAMPION trial (32) randomized a total of 550 patients to telemonitoring with CardioMEMS or usual care. In this trial, CardioMEMS reduced HF hospitalizations with a good safety profile. These results have been reproduced in other studies (33,34). Main limitations of CardioMEMS system include cost and its invasive nature.

In conclusion, more evidence in HF remote patient monitoring is needed. The parameters with stronger evidence for remote monitoring are daily measure of body weight, systolic and diastolic blood pressure, heart rate, analysis of the heart rhythm, peripheral capillary oxygen saturation (SpO2), a self-rated health status and remote monitoring of CIED functions. More data are needed about the prognostic implications of monitoring continuous real-world data and integrating artificial intelligence (AI) models in patient management.

2.3 Technology solutions

The E-health market is on the rise. All reports show that the market will rise more than 23% compound annual growth rate (CAGR) by year 2027, with base year 2020. That is more than 3% per year, a formidable percentage in the COVID age. The same trend is forecasted for the mobile health market: a 17% (CAGR) increase up to year 2028, that is a more that 2% per year. Looking at the quality statistics, an increase of personal health is on the rise. “Health informed individuals” are on the rise and taking more e-health data measures than any previous time in history. It is notable that the younger generation is getting more involved with its personal health than ever before and is using more and more devices and e-health applications than ever before. Finally, the telehealth market is also on the rise. And from the forecast, this segment will have the greatest rise of all. RETENTION project addresses most of the above prediction and current needs that will be described in the following section.

The current section presents the state of art including research outcomes, novel applications and, products in the following technology areas:

- Artificial Intelligence and Decision Support in HF
- Smart home and IoT devices in healthcare
- Real World Data in Healthcare. How real-world data can be compiled and federated?
- Big Data Management and analytics. How and why big data and BI analytics can impact the healthcare setting,
- Human-Computer Interactions. How a modern Human-computer interactions can impact the use of a healthcare system,
- Security, Privacy and Trust in healthcare and IoT systems. The utmost privacy, security, and trust to healthcare system, will be adhered,
- Systems and Applications. What applications and systems will be available for the RETENTION system.

In addition, EU funded relevant research projects are presented and the health landscape needs and policies. The latter includes current patients’ and professionals’ needs focusing on HF,by providing an overview of the health landscape in Europe, trends andhealth system needs .

2.3.1 Artificial Intelligence and Decision Support in HF

The recent onset of Artificial Intelligence (AI) in the cardiovascular field is bringing wide possibilities to physicians from early and more accurate diagnosis to new personalized care. The power to efficiently process different types of data coming from multiple sources -including real world data- from the one side, coupled with the rapidly changing scientific evidence, new drugs and the complexity of guidelines for HF management, especially in outpatient clinic (35) make the use of AI a powerful assistant to clinical decisions and HF patient monitoring. Supplementing or advancing traditional statistical methods, Machine Learning (ML) as a part of AI, implements algorithms to parse data, learn from it, and then make a determination or prediction. In general, ML techniques can be grouped into two sub-categories: supervised learning and unsupervised learning. In supervised learning the model is trained having as input the dataset comprised by instances; every instance has a known outcome (discrete or continuous). On the contrary, in unsupervised learning there is not a single output to predict; the data are unlabeled. The algorithms try to find patterns in the data. Clustering, that is the most common application, uses algorithms that try to group data in clusters based on similarities they may have (36,37). Deep learning comes to exploit computer power for advanced learning using the given data.

Given the nature and sources of RETENTION data, AI and ML can play a significant role in the efficient management of RETENTION patients. In the following paragraphs we summarize recent approached related to the different patient types targeted in RETENTION:

As for the *LVAD patients* RETENTION target group, AI techniques have been utilized consistently to develop risk assessments. (38) applies Decision Trees and other AI/ML algorithms for adverse event risk assessment in LVAD patients also used ML (and main hierarchical clustering) to analyze sequences of adverse events (AEs) after left ventricular assist device (LVAD) implantation. Risk stratification prior to LVAD implantation is also supported by Machine Learning (for example logistic Regression has been used by (John et al., 2021). Bayesian networks have been applied by (39) to get improved prognosis for RV support. Baeysian networks have been applied for mortality prediction (short/long term) (40). Recently Deep Learning techniques have been also applied. For example, (41) have applied a U-net convolutional neural network approach to infection severity recognition on driveline exit site images

In terms of *chronic HF patients* AI/ML have been used for severity estimation. For example, (42) applied Support Vector Machines to stratify patients' status based on major cardiovascular worsening events (with an overall accuracy of 71%), while several approaches stratified patients among different NYHA classes (see e.g. (37,43–45). Tree based methods such as ensemble tree classifier, ROT, random forests, or decision tree based SVMs have been mostly used in these approaches. Apart from their good performance tree-based methods can often offer explainability and these is a reason that they are often preferred from black-box AI based approaches (such as artificial neural network-based ones) that despite their high performance cannot provide an explanation for the suggestion for the recommendation given to the decision maker. The above approaches have used mainly EHR data and data related to medication, condition, etc). Literature reports also previous works based on HRV data (see e.g. (36,46).

AI/ML approaches have been also applied for adverse events of chronic HF patients. Adverse events include mostly hospital re-admissions or deaths. For example, Liu et at applied an ANN approach (with an AUC 64.00%) for prediction of 1-month hospital readmission based on EHR data. EHR data where used by a Generalised Linear Model approach by (47) for 1-, 2-, 12-month readmission prediction with AUC ranging from 61,00 to 71,00%. (48) applied nonlinear XG boost to predict 1-year all-cause mortality prediction (with an AUC of 77,00% while Adler discriminated between high and low mortality risk through a a decision trees

with an AUC of 88,00%. Several works examined both types of events (re-admission/death): for example (49) applied a Cox regression model, (50) examined Random Forests among other algorithms, (35) applied Linear Regression. (43,51) examined different ML techniques with promising results. (see also (43) for a relevant review). Deep learning has been also applied for worsening/readmission prediction with promising results (52).

In terms of *patients with heart transplantation* the last years there is an upcoming use of AI/ML mainly for prediction of survival after a heart transplant, mostly short-term, or high risk complications, a field mainly in its infancy (53). For example (54) developed a risk prediction model utilizing a gradient boosted classification tree algorithm (GBM) to predict the risk of graft failure and mortality 5 yrs. (55) applied AI to identify myocyte damage; the latter is critical for determining the grade of rejection, and thus greatly impacts treatment decisions. (56) applied different algorithms to predict 1-year mortality after heart transplantation. Random forests seemed to have the best results.

Research outcomes as the ones presented above are expected to become the backbone of Clinical Decision Support Systems for Heart Failure. According to (Sutton et al., 2020) 'Computerized clinical decision support systems, or CDSS, represent a paradigm shift in healthcare today. CDSS are used to augment clinicians in their complex decision-making processes'. They can do this by efficiently combining knowledge (clinical) and information from various sources related to patient and environment status. Therefore, a CDSS should combine all relevant information, perform patient centric assessments and presenting recommendations to the physicians. Artificial Intelligence helps towards this direction. Relevant clinical decision support systems have been recently developed in the framework of of EU funded research projects like KardiaTool, SensorArt, SmartTool, HeartMan, HEARTEN. KardiaTool (57)developed a POC solution for the diagnosis and therapy monitoring of HF patients. Combining POC measured saliva biomarkers with additional patient clinical data the so called KardiaSoft decision support system (58) addresses the management, diagnosis/distinction between non-HF (subjects with obesity or hypertension but with symptoms similar to HF) and chronic and acute HF subjects, prediction of adverse events, risk stratification and therapy monitoring advice through visualization techniques. HEARTEN project developed a collaborative environment to empower the HF patients and enhance their adherence in the treatment and lifestyle suggestions. Towards this, a Knowledge Management system applied data mining analysis of multiple information deriving from several sensors, as well as from saliva and breath biosensors. In SmartTool (59)a CDSS was developed based on predictive modelling techniques for HF risk stratification for patients with Coronary Artery Disease. The HeartMan (60)project developed a personal mHealth system for HF patients providing them advice, reminders, and support. SensorArt (61)project focuses on management and remote treatment on patients suffering from heart failure and especially patients with an LVAD. A Decision Support System (38) supports the selection of the best treatment (in terms of LVAD implant or not) as well as monitoring of patient health and prediction of adverse events in LVAD implanted patients.

In terms of commercial products, most existing solutions focus on mainly on management of the patient records and respective visual representation (some of them). Systems such as Dawn Clinical Software (62) , Axis Clinical Software (63) or SpectraCare (64)provide registry management and documentation of key information or electronic health record management. Rimidi (65) remotely measures key parameters and sends encouragement and treatment alteration messages. Lumedx(66) focuses on the healthcare facility; it collects and analyses data to determine facility success. Hospital and re-admission management is offered by CitiusTech (67) although non HF-specific. The CitriusTech platform also performs some readmission risk assessment. Finally, the CareLink network and Paceart Optima System from Medtronic (68) are dedicated

systems to collect information and manage patients with Medtronic devices and provide relevant alert messages.

2.3.2 Smart home and IoT devices in healthcare

In recent years smart healthcare uses a new generation of information technologies, such as the internet of things (IoT), big data, cloud computing, and artificial intelligence, to transform the traditional medical system in one more efficient, convenient, and personalized. With the IoT becoming more prevalent by connecting commercial devices together with the medical field, there are many options to be integrated into smart environments such as smart homes. Smart homes are intelligent structures that use the Internet of Things and embedded devices to increase resident comfort and reduce operation costs by efficiently managing resources (69). The smart home technologies in healthcare can provide some simplified services by collecting healthcare data from devices and help patients that need care to reduce their reliance on health care professionals and improve their quality of life and well-being at home (70).

The medical internet of things can consist of many devices, customized to a user's needs and allowing a smart home environment to accommodate resident safety and health. These devices can be connected directly to the internet through an access point or may connect to an internet enabled device through Bluetooth. Wearable body area networks (WBANs) are a crucial component of the medical IoT (69). Some notable characteristics of a medical IoT integrated into a smart home are the following:

- *Patient safety*: This is the main priority of a medical IoT network. In any sudden event, the system will first attempt to get a response from the patient to reduce false alarms, but if the patient does not respond, a caretaker should be notified. Depending on the severity of the event, emergency services may also be notified.

- *Comfort:* Comfort in a smart building depends on the condition of the environment around the resident. Sensor placement and devices used in a WBANs have a high impact on comfort in a medical IoT network. A consideration toward patient comfort is the effort needed to engage with the devices in the network. Constant and direct engagement with devices creates inconvenience for both users and caregivers. Ideally, maintenance of devices in a WBAN should not complicate a

  user's routine so that the daily routine needs to be designed around constant engagement of devices in the network (71).

- *Design Flexibility*: The smart homes can be adaptable and customized when they use a distributed control system, meaning a system where multiple autonomous control subsystems work towards the same goal under the supervision of a coordinating controller. For example, a controller in the kitchen can control lights, heating and air, while a controller located in a garage can control lights and security system (69).

- *Information and User Engagement*: The user interfaces of apps integrated in the devices allow users to view their data. Patients can be informed on the status of their own care by having the ability to view the data at any time they wish. So, this encourages positive engagement, which leads to a decrease in technology abandonment (71,72).

In Chronic Cardiovascular Diseases (CVDs) there is a major concern about healthcare costs, mainly due to frequent hospitalizations. The HF Guidelines (73) have emphasized the role of daily monitoring of body weight and vital signs. There is a number of noninvasive sensors that are lightweight, wireless, and can be worn by patients to help monitor for abnormal cardiac rhythms, low blood oxygen, irregular movement that may indicate fall injuries, and other symptoms. Many of these devices, and other consumer electronics, are

designed to wirelessly pair with user technology such as tablets and phones to record data that can then be analyzed on a cloud server. The emergence of implantable/wearable smart devices and smart information platforms that can combine advanced sensors, microprocessors, and wireless modules to continuously monitor various physiological indicators of patients, while improving comfort, and allowing the data to be combined with health information is very important in such conditions. For example, in the case of physical inactivity the risk of coronary disease is increased by 45%; stroke by 60% and hypertension by 30% (74), while regular exercise reduces CVD risk (75). Smartphones and smartwatches, which include powerful sensors offers an opportunity to evaluate and monitor cardiovascular health and fitness, through direct measurement of activity allowing real-world measurements of physiologic parameters (76–78). In the study of *MyHeart Counts* Cardiovascular Health (79) 50.000 individuals recorded daily physical activity, sleep and cardiovascular health data using an iPhone application via Apple's ResearchKit framework contributing to the research community to a better understanding of the relationship between cardiovascular indicators, lifestyle, and overall health, as well as inform mobile health research best practices. Relevant EU funded research projects such as SMART-BEAR(80) aims to integrate heterogeneous sensors, assistive medical and mobile devices to enable the continuous data collection from the everyday life of the individuals. The provided Smart Home solution will seamlessly integrate both smart home devices and healthcare-enabled sensors in a personalized environment where each person will be supported by artificial intelligent technologies.

The disease management programs for HF patients supported remotely are not only effective but also economically advantageous. Benefits are huge, with a 30–35% reduction in mortality and 15–20% decrease in hospitalizations [13, 14]. The use of the smart devices in the context of telemedicine allows for early identification of symptoms or signs of HF and prompt intervention. Clinical parameters (weight, BP, HR, SatO2) and ECG signal, along with some descriptive indices of health status (score of fatigue, dyspnoea and peripheral congestion) can be monitored at the patient's home.

In addition, environmental sensors including temperature, smoke, humidity, water, and gas detectors may also be part of the integrated monitoring system. Smoking increases the risk of lung cancer and respiratory disease, but also nearly half of the premature mortality associated with smoking is due to CVD. Smokers have a nearly 2-fold higher risk of coronary disease and a 10-fold higher risk of developing peripheral artery disease. Smokers are also more susceptible to arrhythmias, stroke and sudden cardiac death. Smoking decreases regional left ventricular function even in asymptomatic individuals and significantly (45–80%) increases the risk of heart failure(81).

All the studies highlight the necessity of further deployment of smart home and IoT devices for enhancing the healthcare experience as part of the progression of digital, remote, connected and virtual care.

2.3.3 Real World Data in Healthcare

Real World Data (RWD) defines collected data derived from a various number of sources, such as patient registries, health records (e.g., EHR), health insurance databases, pharmacy databases with billing data, biometric signals captured by mobile devices or watches, or additional non-medical sources like social media, economic outcomes, or any source type that do not originate from conventional clinical trials and help assess potential developments of patients' health state and quality of life.

The most used big data sources are described in what follows.

EHR data

Murphy, Hanken and Waters (82) have defined the EHR as a notion which is associated to the collection of all the medical records of patients, from past to present and even future prognosis. These records can be

used to provide patients with correct and prompt medical services. This type of data comes from various sources like laboratory testing, admission notes, procedural records, patient's medical history, diagnosis medications or radiology images. The EHR data are not collected with aim to create datasets for research purposes, but rather the intent is to document and perform administrative tasks to improve patient safety and optimize healthcare delivery. Therefore, EHR data may lack the standardized way of structured datasets in which the focus is on the analysis to be performed upon. However, there are studies to improve the data coming from EHRs, so that the information could serve better for further analytics (83). Recent advancements based on EHR data for health interventions are undertaken also by European projects, e. g., the EHR2EDC (84) project which demonstrates a method to automatically transfer patients EHR data to Electronic Data Capture (EDC); the EHDEN (European Health Data and Evidence Network)(84) project, a federated network of databases designed to unify data models; or Sentinel(85) initiative, a framework that transforms the way researchers monitor the safety for FDA-regulated medical products.

Clinical registries

Registries such as American College of Cardiology (86) collect structured data using standardized procedures. One of the many purposes of these repositories is to provide a benchmarking quality factor for the participating units. One important limitation is that data collection is partially handled by EHR, which may introduce the EHR issues related to unstructured format of the data.

Biometric data

Biometric data can be acquired from IoT devices such as wearables. For example, Fitbit and Apple's ResearchKit (87) provide researchers access to vast stores of biometric data on users, which can then be used to test hypotheses on nutrition, fitness, disease progression, treatment success, and the like. The best example so far is the Apple Heart Study(88), for which 400 000 participants delivered data to researchers. Yet this study lacks to provide insight to arterial fibrillation, is still a good example that one can use HealthCare Big Data systems for various cardiology research.

Dealing with real world data faces an important issue regarding its structure which varies from type to type and from one medical recording unit to another. For this reason, it often needs significant effort in pre-processing before its use for analysis purposes. Useful relevant information has been successfully extracted in this regard, using natural language processing techniques (89).

2.3.4 Big Data Management and analytics

'Big data' represents substantial amounts of information collected, stored, and organized from various sources which are complex and hard to manage with traditional technology (90).

Huge amounts of data are collected over the years from patients or visiting patients in clinical institutions in rather distinct records with almost no possible data connectivity to draw any conclusions, make connections across distinct patients, or investigate other illnesses cause factors such as parameters from real world data. The available technologies nowadays can screen zettabytes of information in amazing short amounts of time, which offers the possibility to create complex reports and insights not possible before. At this point, healthcare analytics can predict and offer solutions to a disease or a risk case, early in time and has the capacity to evaluate treatments with a faster pace, have a better track of data inventory and acts proactively with suggestions towards individuals for improving their health.

In more specific terms, the modern computer systems and applications have made possible the digitalization of various medical services, for example, the storage of medical records that can facilitate a general view of the patient's health, resulting in vast amounts of data. In this sense, smart AI algorithms like neural networks help achieve real-time automated decision-making improving and even saving patients' lives.

In the healthcare domain, different important sources are used for acquiring 'big data': ranging from real world data, like patient's insurance data and medical history (diagnosis and prescriptions) to medical and clinical data (e.g., laboratory examinations, genetics, genotyping), and supplemented by other private or personal medical data (such as lifestyle habits, dietary factors). Smart DSS can integrate all this acquired data and process it to provide the best medical services to the patients and provide personalized treatments.

Commercial existing AI platforms for healthcare big data

Treating big data challenges and implementing smoother analysis, several companies and start-ups have used AI for commercial healthcare solutions in the last years (90). For example, IBM's Watson Health(91) deals with health data passed between providers, hospitals, and researchers. As Dash et al. describe in their review (90), various other platforms provide big data health analytics and management solutions based on ML intelligence. For example, MedeAnalytics(92)uses extended history of patient data, while OptumHealth (93) improve e-health system's infrastructure for the healthcare industry. Health Fidelity(94) also provides management solutions and optimizations but for risks assessment within healthcare organization workflows. Another AI platform, Flatiron Health(95) focuses on oncology research for providing better treatments. Enlitic(96) uses deep learning methods on large-scale clinical tests for providing healthcare diagnosis. Digital Reasoning Systems and Apixio (97) offer cognitive computing services and data analytics solutions for making sense out of highly diversified data, further integrating clinical data and health records. Linguamatics(98) is another text mining platform dealing with unstructured healthcare data. And big companies such as Oracle Corporation and Google Inc. contribute to the healthcare development by providing cloud-based storage platforms with distributed computing power, necessary for big data management.

Challenges associated with healthcare big data

Despite the various sources and the huge amount of acquired data, another important problem arises. All this data is unstructured and hard to correlate and use. This issue is generated by the many different formats used to acquire the health information and the impossibility to use a pre-defined model. The unstructured nature and the subjectivity of health data, like patient's lifestyle conditions, socioeconomic parameters, and patients' personal reports, lead to the storage of data into unstructured formats. The integration of such different data sources into one general used format is difficult, but vital to further process the data and generate correct and helpful predictions for the patients' health. Other issues relate, for example to data cleaning to assure correctness and consistency, non-unified formats, data discrepancy, security (breaches, hacking, phishing attacks), incomplete or inaccurate meta-data, improper interoperability between datasets, lack of interoperability in data sharing, improper data visualization which induces confusion, or technology limitations in data processing in terms of memory (90). For clinical settings, another major challenge arises regarding the implementation of high-end computing tools, protocols, along with the necessity of high-end hardware use.

Big data analytics solutions

For developing a healthcare system based on big data providing trustworthy, meaningful information and fast decisions, the challenges need to be overcome. The multiple challenges faced when using bigdata and analytics can be treated to some extent with common data analysis techniques such as: dimensionality reduction, Machine Learning model building, or Deep Learning(99). Having better diagnosis and disease predictions will not only improve patients' quality of life, offer real-time feedback, but also importantly

reduce costs, time, and hospitals overload. Further, big data analytics could play a role in optimizing hospital staff and operating rooms necessities or improving pharmaceutical supply chains.

The majestic deal that AI brings, is handling anomalies in mountain piles of data and at the same time meaningfully interpreting the data without bias as in the case of human expertise and even capture related health conditions (100). It can analyse results of specific treatments, recovery times from an incredible number of patients in no time, from different locations. AI can help in improve the time for diagnosing a patient. For example, an OCR system can recognize the handwriting, helping at optimizing the digitization of one entire procedure. A prediction model can detect abnormalities, helping at pinpointing to the healthcare professional the cause of the patient's illness. NLP tools can generate new documents or dictate clinical notes while the doctor is performing a procedure.

Management and analysis of big data

Loading collections of big data into memory is inefficient. The solution is to process the amount of data in parallel on several clusters, which is the solution provided by the Hadoop framework (101). Sometimes, due to the large size of data, the MapReduce algorithm maps each logical record into a dictionary of key/value pair to reduce the operations that share the same key. This system is scalable, efficient, and robust, thus popular companies have adopted it to handle their data. Another alternative to Hadoop is Apache Spark, a unified engine that handles distributed data processing by implementing a new architecture namely RDD (Resilient Distributed Datasets), hence, Spark(102) can be hundreds or more times faster than Hadoop; the only downfall of this approach is that Spark will require huge amount of RAM memory which can raise the costs when using such system. Kafka platform handles real-time data streams and performs well in aggregating inconsistent data from many different systems, can handle multiple consumers very well, offering durable retention, is scalable and comes with high performance (103).

Big data implications to Heart Failure (HF)

Detailed and accurate vast amounts of data, together with the boost in AI development, helps nowadays diagnosing and predicting HF with a success rate and a speed way higher than trained experts (104). Smart big data systems (105), can help in discovering new hidden risk factors of CVD (106) or predict the risk of bleeding and stroke using patient personal data like hypertension values, abnormal renal function, abnormal liver function, age, drug therapy and alcohol intake scores and even facilitating treatment doses and further patients' recovery.

In respect with public health, several approaches tackled various methods of applying big data analysis in heart diseases prevention or abnormal events detection which could save lives, e.g., as in the case of congestive heart failure prevention where high accuracy is reached as never achieved before(107). Multiple data variants can be integrated using the machine learning technique termed tensor factorization, to derive clinical heart failure with preserved ejection fraction (108) and have significant impact in underlying pathophysiology and differential response to therapies.

There are a few big data systems that are currently applied in clinics: for example, various types of omics are used to determine acute allograft rejections(109). Heart failure is a hot topic for big data research because of the high complexity of the syndrome, the various numbered of risk factors, and the high degree of patients that suffer from this disease. Within the Medolution Project (110), LVAD (left ventricular assisted device)

patients are considered, where besides a GUI application that allows a permanent and continuous contact between patients and the physician, there is a big data analysis system that runs permanently and detects abnormalities or other events which impose immediate reaction. High dimensionality vectors created from large quantity of data gathered from hospitalized patients, applied on an automatic learning model, were used to predict cardiac amyloidosis which is a condition of the heart tissue which must be detected early. Because many patients received incorrect diagnose in the past, a new method is proposed by Garcia et al.(111), by using statistical learning algorithms that help detecting this disease.

New approaches use real world data (RWD) for HF prediction (112–114), to supplement the standard clinical trials outcomes and help assessing new treatments for improving heart failure conditions. However, since distinct treatments schemes must be examined in parallel to compare their distinct values, which involves voluntary patients, longer time, different parameters to be set, trials approvals, ethical implications, and so on, few evaluations have been performed yet. The common sources consider EHR, omics, clinical data (e.g., patient demographics, hospitalizations, comorbidities, mortality, left ventricular ejection fraction, etc.) (115). Challenges observed relate to the quality of healthcare data, lack of consensus on phenotyping diseases in RWD, harmonising and standardising data and incomplete data collection. However, these could be tackled with data mining techniques and ML algorithms so that even sub-phenotypes of heart failure can be then predicted from EHRs(113).

2.3.5 Human-Computer Interactions

Human beings need to process information fast. Even though Computers are data transforming machines using algorithms, sometimes challenges to the design of the User Interface (UI) can create frustration to the users. The study of Human computer interface (HCI) can solve most of the problems concerning the interactions of Man and machine. The increasing use of information technology in all aspects of our lives, creates a new reality to all human endeavours and it is truer every day that goes by. The use of a multitude of information in the any context, can be detrimental to our success, as professionals or in our personal interactions and well-being. Healthcare creates a new and very promising landscape for information technology. In these context, Human-Computer Interaction (HCI), becomes more and more important to clinicians, patients, and everyone in between.

Health care services present a multitude of inconsistencies: there is a substantial investment in innovative health technologies, but most systems that are currently deployed, are difficult to use. At this time, a major shift is happening in healthcare industry: care and decision-making being delivered by a clinical professional is moved to the patient, which is expected to be well informed and be able to be actively engaged and involved in shared decision making with the clinical professional.

From a technical perspective, this can be achieved by novel information technologies, like innovative human computer interaction, real time data collecting, hand-held device connectivity (IoT), body attached devices (smart watch), modern Personal Health Records (PHR), etc.

Several barriers exist in the provision of user-friendly interfaces for the connected health applications, such as:

1) low health literacy increases difficulty in explaining medical conditions, medication suggestions and treatment options.

2) age-related conditions (e.g., hand–eye coordination decline, cognitive deterioration, etc) must be considered during the design of interfaces, and

3) complex big volumes of raw health data need to be visualised to users of different backgrounds. Human-Computer Interaction (HCI) plays a major role in delivering the results of digital technologies to the healthcare sector.

4) Low computer literacy or denial of use: it is fact that some people either are technology deniers and don't like to use computers (tablets and smartphones included) in their daily life.

However, the perceptible impact of HCI on healthcare practices and on the experiences of health professionals and patients has been relatively limited to date due to challenges in healthcare related to data volume, privacy, treatment complexity, disperse technologies and multi-purpose interactions with data among others. Therefore, an assessment of user needs is critical to the interface design of a new health information technology application [90 of GA]. Lifestyle, disparities, technology access, impact of chronic conditions and health literacy are some of the factors to consider. Towards an effective HCI design, the aspect of mobile devices being a rapidly growing medium of interventions [92 of GA] must be considered. Touch-screen interactions and standardised ways of obtaining self-reported information about QoL are also confirmed to lead to high acceptability rates by patients [93 of GA].

Key issues about HCI that RETENTION addresses:

1) involve the users (from patients to clinicians) in all stages of development and

2) evaluate the system from the user point of view, using the System Usability Scale (SUS) by John Brooke in 1986 and 1996 ("SUS - A quick and dirty usability scale" - Brook J. - 1996).

System usability Test and scale, evaluates a system in the following term:

1) Efficiency

2) Intuitiveness

3) Ease

4) Satisfaction

2.3.6 Security, Privacy and Trust in healthcare and IoT systems

Internet of Things (IoT)-enabled devices provide means for remote monitoring of individuals health indicators, while can empower clinical case managers, caregivers, and other health professionals to analyse real-time conditions and to deliver personalised care, more efficient, faster, signifying impact on reducing healthcare costs and improving the accuracy of the interventions. Still, technical aspects tied with such endeavour should be closely monitored since every single IoT device and their connectivity functionality introduces a certain degree of security and privacy risk as several studies (116) on security vulnerabilities at the hardware level, protocol-level, and application-level of IoT indicate. (116) states that the exploitation of the known IoT-related vulnerabilities can be prevented by taking several countermeasures against each of the exploits, and in this context ENISA has been establishing secure development guidelines across the IoT ecosystem for achieving security by design (117), in parallel with domain-specific cloud security best practices

(such as the one for the healthcare industry (118). Within the context of RETENTION, the following technology aspects pose challenges that will be closely monitor due to the design complexity of medical devices and their management (e.g., ventricular assist devices (VAD), left VAD, right VAD, bi-ventricular assist devices (BiVAD).

IoT devices security risks

Each RETENTION IoT device (i.e., Internet of Medical Things (IoMT) technology for connecting medical devices, personal wearables, smart home sensors) using a wireless technology standard to operate and transmit indicators (i.e., raw/aggregated health data), introduces a vulnerability security risk. While for the common devices (e.g., smartphones, laptops, or tablets) to be used for running the clinical study application (RETENTION app), vulnerabilities are well known (or at least new security weaknesses/threats are reported along with easy-to-do fixes) and as such easier to spot and repair, the same cannot be said for IoT devices, for which due to technical constraints (e.g., compact size, energy consumption limitations) are not designed with security top of mind and consequently are posing a greater security risk.

In addition, for most of IoTs in the healthcare domain and those of RETENTION, there's no certification for cyber security even though they are dealing with medical indexes (Regulation EU 2017/745 refers to CE certificates and requirement for medicines with an integral device, still without specifying a certification mechanism). To this end, in addition to closely monitoring interoperability channels to be used (e.g., Bluetooth v4) to minimize risk of intercepting its communications, attention is also required in the process of de-associating the generated data, so that even in case of a data loss such incident (caused by a IoT or smartphone's malfunction or bad practice) this will not lead to identification of the end-user. This dimension should be considered especially in cases when IoTs are operated by end-users who do not have a technical background for operating such devices (as in the case of RETENTION), and when it is almost impossible, due to the large number of devices, to keep close track of what it's going on for every IoT device for a significant period (e.g., one year). As an effective countermeasure, a monitoring mechanism that is aware of when each device (i.e., IoT, hub, smartphone) accessing the network or equivalently transmitting data can assist in identifying potential vulnerabilities and/or basic malfunctions (RETENTION platform), while data-collectors' applications (RETENTION app) could be equipped with updating (e.g., patching software/firmware upgrades) mechanism to minimise known threats.

IoT usage data stored

As stated in the DoA, the RETENTION platform will use state of the art technologies for big data management, data analytics, and AI-enabled decision making to assist the delivery of personalised interventions for HF patients. This platform should preserve the security and privacy of the sensitive personal and clinical data that it will collect, manage, and analyse. By extending the boundaries of this requirement, the whole RETENTION project is motivated by the need for personal data management and services that comply with the General Data Protection Regulation (GDPR 2016). GDPR grants the industry the ability to create knowledge derived from (personal or not) data analysis, provided the data subjects are given control of knowing and administering who and how their data are being processed in a verifiable way. Adhering to this regulation, the "Privacy by design" principle will be embedded into the architecture of RETENTION platform and the RETENTION app, while specific features will guarantee the exercise of GDPR rights by study participants. By adopting such principles, even in the unlikely event of malicious access to the RETENTION repository(-ies) is achieved, or data are leaked by a system administrator's negligence/error, still this design concept guaranties that will not be possible to reidentify study participants.

The challenge lies in introducing data management concept that will assist achieving project's goals while preserving privacy, and as such ensuring study participants (that provided their consent) about the security and privacy of the data held in the RETENTION platform and the protection of the platform itself. In this context, having a system that, as a fundamental requirement, is designed in such a way that the full length of the collected or produced Big data (i.e., usage data, medical data, resulted analytics and interventions) should be kept in a anonymised fashion, while a small subset consisting of IDs and Personal Identifiable Information (PII) as far as it concerns participants (study patients), and login-profile information of the end-users, stored with high security safeguards (i.e., encrypted, logged and limited access to specific role(s)), prevents in principle the association of leaked data with study participants (e.g., IDs management introduced in EVOTION (119).

AI analytics

Considering the scope of RETENTION through the use of the AI (e.g., human oversight, decision making, protection of personal data), it is intended that the project looks into these aspects and address them in an appropriate manner. Data will be provided by the study participants on a voluntary basis, in accordance with well-defined informed consent procedures, goals of data processes and individual's rights. In principle, RETENTION data and resulting analytics and interventions will not consider any personal, discriminative references. As such, there is no risk of discrimination due to data processing conduct in the context of the study.

Basic requirements

More specifically, RETENTION project will take into account a series of instruments of horizontal relevance, as well as sector specific. It will, therefore, consider the following regulations and soft law instruments linked both the performance of scientific research in the context of Horizon 2020 framework and to the scope of RETENTION per se:

- The Convention for the Protection of Human Rights and Fundamental Freedoms
- The Charter of Fundamental Rights of the European Union, specifically Article 8 concerning the protection of personal data.
- The Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data (General Data Protection Regulation).
- The Regulation (EU) 2019/881 of the European Parliament and of the Council of 17 April 2019 on ENISA (the European Union Agency for Cybersecurity) and on information and communications technology cybersecurity certification and repealing Regulation (EU) No 526/2013 (Cybersecurity Act).
- The proposal for a Directive COM/2013/048 of the European Parliament and of the Council of 7 Feb 2013 concerning measures to ensure a high common level of network and information security across the Union, with special focus on Article 9 concerning secure information-sharing systems.
- The Directive (EU) 2016/1148 of the European Parliament and of the Council of 6 July 2016 concerning measures for a high common level of security of network and information systems across the Union (NIS Directive).

- The Regulation (536/2014) of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC
- The Ethics Guidelines for Trustworthy AI, High-Level Expert Group on Artificial Intelligence set up by the European Commission, of 8th April 2019.
- The European Union Agency for Cybersecurity ("ENISA") Handbook on Security of Personal Data Processing (2018) and the Handbook on Cloud Security for Healthcare Services (2021)
- Other soft law instruments governing scientific research, such as the European Code of Conduct for Research Integrity, the Guidelines to rules on Open Access to Scientific Publications & Open Access to Research Data in Horizon 2020, the Guidelines on the Implementation of Open Access to Scientific Publications & Research Data in projects supported by the European Research Council under Horizon 2020, and the Guidelines on Data Management in Horizon 2020.

As from the 26th of May 2021, manufacturers of medical devices must comply with the Medical Devices Regulation (EU) 2017/745 (MDR), at the Article 2 (1) of which it is specified that software is included in the definition of (medical) devices. The RETENTION platform will operate under certain instructions that process input data (collected by heterogeneous resources) and create output that will be used to inform the clinical management of patients with chronic HF. It will also analyze these data in an anonymized form using AI-assisted analytics and decision models to generate evidence useful for making public health policy level interventions. It is, therefore, important to clarify whether the software developed for the RETENTION platform may be qualified as a medical device software, and thus be subject to the medical devices' regulation. In that case, the impact of the MDR in the context of the consortium obligations should be considered.

In this regard and following the MDCG 2019-11 Guidance on Qualification and Classification of Software in Regulation (EU) 2017/745 – MDR, it should be pointed out that, although the actions performed on data by the RETENTION software will not be limited to mere storage or communication of data and that the results of the data processing will be used for the benefit of individual patients, it may not necessarily be qualified as a medical device. The relevant, here, condition is whether the software will be used for the medical purpose of "*diagnosis, prevention, monitoring, prediction, prognosis, treatment or alleviation of disease"* (Art. 2 (1) 2017/745). The monitoring, though, of the patients will be carried out via -amongst other means- already commercialized in the EU market medical devices which operate independently and with which the RETENTION software will interact to obtain input data. Notably, in the context of the project these devices will not be used "off-label" and no investigations on these devices as such will be undertaken. As the RETENTION platform essentially gathers and centralizes the various patient's data, the purpose of the software under consideration may not be acknowledged as a medical purpose per se. Additionally, the RETENTION platform will not create additional and immediate decision-triggering information, in the sense that, apart from the aforementioned point on the acquisition of the medical information process, the platform will only provide indications deriving from the presented gathered data. These will be at the medical professional's disposal to evaluate, validate, and possibly inform clinical decision-making.

Having made this preliminary analysis on the (non-)applicability of the MDR to RETENTION, following reservation must be expressed. According to the definition of the "manufacturer" of the MDR (Art. 2 (30)), to be qualify as a manufacturer of a device, one should manufacture and place the device into the European market under its name or trademark. In the case under examination, the RETENTION consortium acts as the contractor of the European Commission (under the RETENTION GA No. 965343). In the context of the consortium's obligation to exploit the project's results (Art. 28.1 of the GA), appropriate measures must be

taken to -amongst other possibilities- market the project's products. It is therefore acknowledged here that the European Commission, as the manufacturer, has the final word in deciding if the design and manufacturing of the RETENTION software should fully comply with the requirements of the MDR -namely, to otherwise qualify the platform- in order to be placed on the EU market.

Further to the above legal requirements and in order to combine them with technical ones, it should be taken into account our RETENTION proposals. Thus, the RETENTION system will collect, store, and transform data into valuable information and decisions. This fact creates a mandate to the system and the system designers, to create a fully secure and at the same time functionable system. So, a key objective of RETENTION is to provide a trustworthy platform with security and privacy provisions considered by design and maintained throughout the development, testing and refinement of all components comprising the solution. The provisions adopted will be proportionate to the highly sensitive data involved in the operation of platform and the relevant safety, regulatory, legal, and ethical issues resulting from the healthcare environment. State of the art controls and processes will be adopted in RETENTION to ensure that all security, privacy and regulatory compliance requirements, as identified by the comprehensive risk and compliance assessment carried out at the early stages of the project.

Also, the Consortium beneficiaries will establish and operate continuous security and privacy assurance checks for the RETENTION platform, i.e., mechanisms that will support periodic vulnerability analysis, penetration testing and continuous monitoring of the implemented security and privacy control mechanisms of the platform to ensure the security and privacy posture of it, and generate evidence that can demonstrate this posture to different stakeholders (including users, patients, clinical experts and regulatory authorities).

The RETENTION system will deal with two important categories of Data:

- Personal private data private, like first name, last name, date of birth, social security number, etc., and,

- Sensitive private data, like biometric, diagnosis, tests, prescriptions, doctors' orders, results, etc.

The RETENTION system will be able to have secure ways to handle, distribute, and show information, to the correct set of 'eyes' (the correct individuals), without compromising usability or speed. Great detail will be given to some elements of this data, such as details of Patient Records, that can be categorized as *Personally Identifiable Data*, i.e. information that can be used to uniquely identify, contact, or locate a single person or can be used with other sources to uniquely identify a single individual. This data will be 'hidden' and protected as much as possible, and even at the event of security leak, the system will be designed is such a way that the minimum amount of data will identifiable. In addition, ethical issues in specific will be addressed through the ethics approval application process and the continuous ethics monitoring in the project.

The security of the system and the protection of personal and sensitive data will occur in full compliance with the GDPR rules, as it is a key requirement of the project but also an important risk factor in case of non-compliance with legal and other requirements. For these reasons, the risk will be assessed for the new information system, by considering the EU directives, the national legislation of each country, the requirements of the Data Protection Authorities of each participating country and the entire legal and institutional framework that governs the operation. It should be noted that the consortium has significant experience in the development of polar security but also in its implementation, thus ensuring the coverage

of all the relevant needs of the project. For the whole duration of the project, data will be managed as per the requirements of the GDPR and/or any other applicable local legislation.

For external systems that might be connected to the RETENTION, special care will be taken, so data that flow from one system to another will be fully secured and there will be no identifiable data transfer. The transfer and use of data between systems will be enabled between RETENTION and other specified and named systems of the entities involved in the project. During normal operational support, the transfer with the associated systems will be covered by the Data Protection principles defined by the GDPR regulation. Therefore, any activity which requires the RETENTION consortium to exchange service-related data, the service shall be in line with the requirements of the specific regulation.

The capturing, processing, output, and transfer mechanism of all data will conform to the EU GDPR and local security policies and must be in line with the latest ISO 27001 / ISO 27799 standard principles. Encryption of the data in storage or whilst in transit shall be applied if this exercised to an outside system or network. The data shall be used only for the purpose for which it is requested to be utilized, including and applicable to the consortium. The consortium maintains this responsibility for the resources deployed.

The host institution will confirm the appointment of the Data Protection Officer (DPO) and the contact details of the DPO will be made available to all data subjects involved in the research. For other institutions not required of a DPO, a detailed data protection policy for the project will be kept on file and submitted upon request. All the data they intend to process is relevant and limited to the purposes of the research project and only. Also, security measures will be implemented, to prevent unauthorized access to personal data or the equipment used for processing. Anonymization techniques will be implemented, so data will be identifiable. And finally, the beneficiary will provide a confirmation via informed consent, that it has a lawful basis of data processing.

Another aspect of security will lay in the architecture of the system. Security and privacy will be a primary concern when designing, developing, and operating the RETENTION platform: the multiple entities and complex interactions expected during the use of the RETENTION platform, including the various Machine-to-Machine (M2M) and Machine-to-Human (M2H) at the RETENTION Edge instances, the RETENTION CSB instances, and the RETENTION GIC, as well as the interactions between these layers (i.e., communication between Edge and CSB instances, and between CSB instances and the GIC). In all cases, the intricacies of the different devices, as well as the different entity roles (e.g., patients, caregivers, clinical experts, administrative staff, data scientists), will be taken into consideration. A strong, dynamic and seamless Authentication, Authorization and Accounting (AAA) mechanisms will be integrated for the protection of all M2M and M2H interactions involved. Security (i.e., confidentiality, integrity, and availability) of data at all states (i.e., at rest, in processing and in transit) will be provided, leveraging industry best practices and standardized mechanisms, along with the definition of a secure-out- of-the-box configuration for all deployed components. The aim will be to provide a trustworthy platform with accountability provisions, as this is not only a prerequisite for its wide adoption, but also mandatory from a regulatory, legal, and ethical perspective.

Connection to Internet and/or other private networks and under constant barrage from worms, viruses, and targeted attacks, the organization must be vigilant in protecting the network infrastructure, user data, and customer information. Additionally, multi-layered network will utilize security zones so as granular security policies can be implemented at the different network layers. Offered security services can set in place proper physical separation (zones) and filtering between hardware servers that will be accessed by internet users versus those hardware servers that will be accessed by the intranet and WAN users. The network usually is

divided into three major layers. External, DMZ and Internal which can further have subdivided according to the N-Tier model.

The Security Assurance platform will be used also: combines runtime monitoring and dynamic runtime testing to ensure to correct and effective operation of security controls in cloud and distributed systems and will be hooked to different systems programmatically through probes to monitor the communications. Finally, Differential Privacy to enable the processing of data in a secure and trustworthy manner at the RETENTION GIC, especially regarding interactions between external entities with the platform.

Finally, security is an integral part of the infrastructure deployment. The need to have secure and reliable infrastructure, protect information assets, and meet regulatory compliance requirements, the solution will deploy security services designed into the network rather than added on as an afterthought.

Considering the complexity of the legal environment about human rights and GDPR, and the technical intricacies of the system, the consortium will apply all scientific, technological and law expertise to create a system that will be totally secure, private and at the same time useful to the users.

2.3.7 Applications

Mobile Health (m-Health) is an emerging e-Health technology developed because of improvements in information and communication technology. m-Health delivers healthcare services electronically, overcoming geographical, temporal, and organizational barriers. The applications (apps) of m-Health address emerging problems in the health services, including the increase in chronic disease related to lifestyle, the high costs of the national health services, the need to empower patients and families to handle their own healthcare and selfcare, and to provide them with direct access to health services, regardless of time and place. Nowadays, smartphones are widely spread and its use in remote patient monitoring is promising. However, lack of efficacy testing is one of the biggest barriers to adopting mobile Health apps.

Nowadays, smartphones are widely spread and its use in remote patient monitoring is promising. However, lack of efficacy testing is one of the biggest barriers to adopting mobile Health apps. Most of studies have a small sample size and are observational studies. Several reviews and meta-analysis have been published (120–123). These publications pointed the main problem in mobile health apps for HF: the wide range of technologies (including invasive devices), provider response, duration and health outcomes assessed made meta-analysis difficult. Therefore, the quality of evidence in this field is very poor.

Some of the most popular mobile apps for HF patients are:

- **Health Storylines**: This is one of the most complete apps. Developed by the Heart Failure Society of America. Available for iOS and Android. The app has several options for different diseases including HF. If you select HF settings you can track body weight, heart rate, blood pressure, waist circumference and blood sugar (if diabetic). In this app the patient can also find:
    - symptoms tracker
    - medication reminder
    - appointment calendar
    - educational contents

- exercise diary
- chat with other patients
- generate PDF about patients health status
- share patient´s progress with relatives/friends.

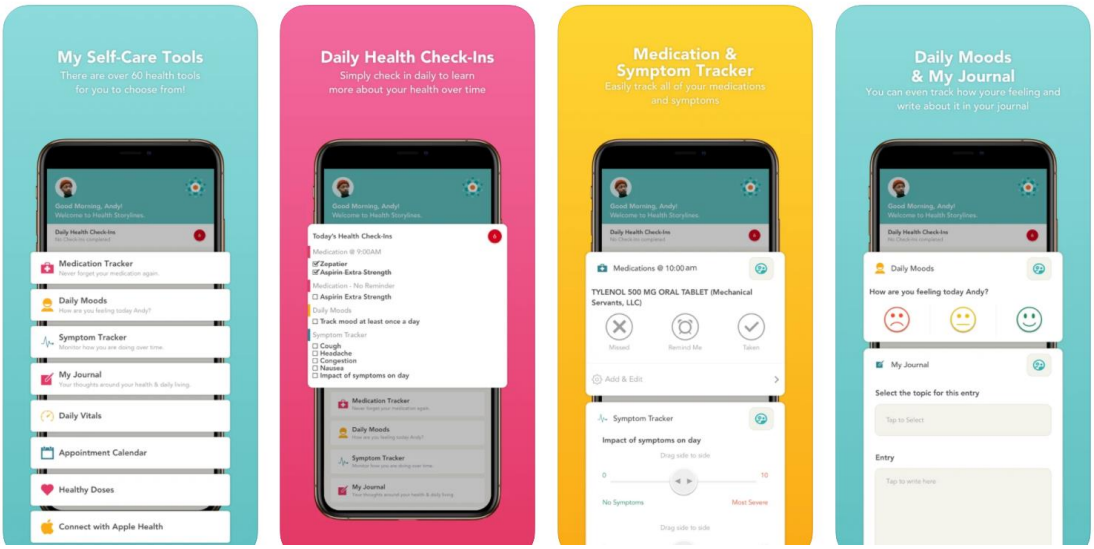

Figure 3. Health Storylines screen shots.

- **HF Path:** developed by the American Heart Association. Available for iOS. At the time of this review the app has been removed from apple store. The app teaches patients to track and manage their symptoms, weight, and medication regularly, while also educating them to take small steps to improve their quality of life through engaging interactive courses.

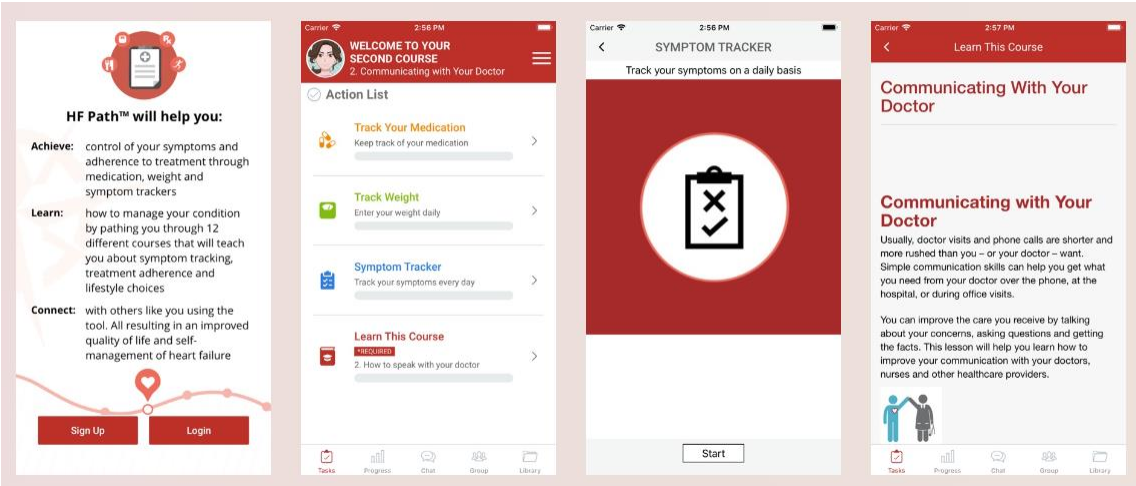

Figure 4. HF Path screenshots.

- **Heart Failure Manager @Point of Care:** Available for iOS. This app allows the interaction with apple watch to access to more complex data such as heart rate or AF detection. In this app the patient can:
    - Track his progress and symptoms by filling in the daily journal with its sliders and buttons and watch his data transform into easy-to-read charts
    - Manage his medications and treatments, including reminders
    - View/share detailed records on heart rate activities provided by Apple Watch and other devices
    - Use the photo upload feature to share visible symptoms with care providers
    - Connect to care providers so they can monitor his progress between visits and better understand how your condition is affecting you
    - Stay up-to-date with the latest information on Heart Failure when he access the "Learn More" section

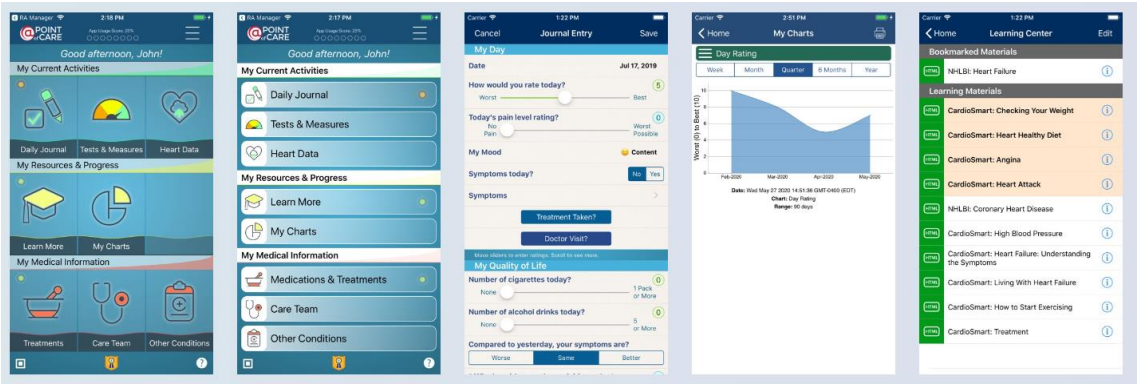

Figure 5. Heart Failure Manager @Point of Care screenshots.

- **My Therapy:** Available for Android and iOS. One of the most popular health app with more than 1 000 000 downloads. This app is focus on medical adherence but it also provides a tracking of blood pressure, saturation, weight or sugar blood levels. In this app the patient can:
    - Injection site tracking
    - Reminders for all his medications
    - Pill tracker with a logbook for both skipped and confirmed intakes
    - Support for high-complexity dosing schemes
    - Track his tablets, doses, measurements, and activities
    - Refill reminders when he is running low
    - Connect with friends and family for encouragement
    - Share his printable health report with doctors

- Record his symptoms and well-being
- Receive personalized tips for his treatment
- Wide range of measurements for all conditions (diabetes, rheumatoid arthritis, anxiety, depression, hypertension, multiple sclerosis), e.g. weight, blood pressure, blood sugar levels

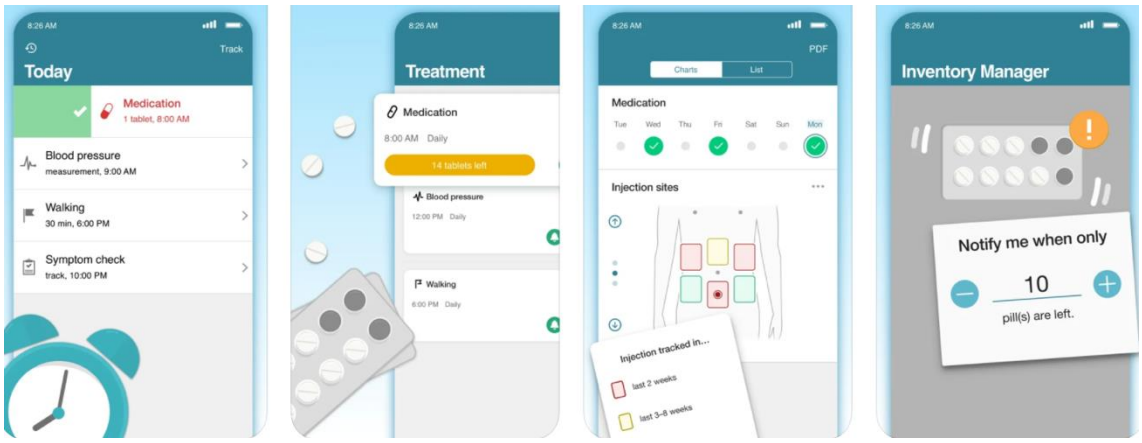

Figure 6. My therapy app screenshots

- Beurer Health manager: Available for Android and iOS. The app is designed to tracking weight, blood pressure, blood glucose, activity, sleep and saturation. It allows Bluetooth connection with Beuer products.

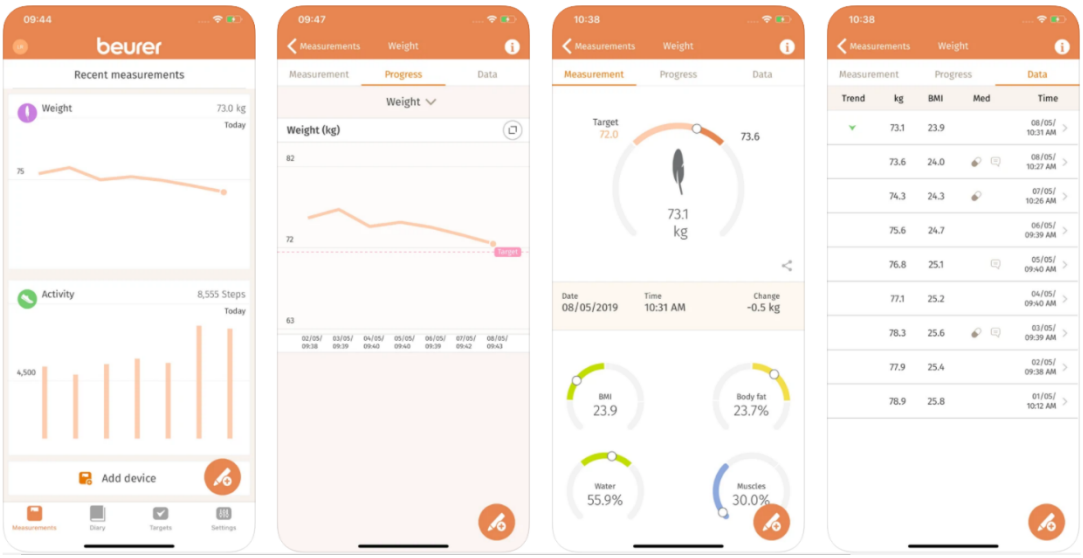

Figure 7. Beurer Health manager screenshots

2.4 EU funded relevant research projects

Several EU, national and international R&D projects and initiatives investigate topics relevant to RETENTION, while some of the RETENTION partners already participate in these EU projects. As far as it concerns projects running that are related in the RETENTION domain and/or produce outcomes that may interest RETENTION and can be exploited, the following are presented in detail in D9.2 (see Section 4.7 Synergies with other projects and initiatives):

- UNITI (https://uniti.tinnitusresearch.net/)
- SMART BEAR (https://www.smart-bear.eu/)
- EVOTION (https://h2020evotion.eu/)
- HOLOBALANCE (https://holobalance.eu/)
- I-BiDaaS (https://www.ibidaas.eu/)
- sustAGE (http://www.sustage.eu/)
- SENSE-Cog (https://www.sense-cog.eu/)
- IMPILO (https://www.datamed.gr/impilo)
- TRANSITION (https://www.datamed.gr/transition_)
- Obesity (https://www.datamed.gr/pedobesity)

Exploring synergies with those (due to the direct involvement of RETENTION partners) as well as other H2020 projects, national initiatives, and networks (aforementioned below), will ensure promotion of the RETENTION outcomes through the channels and services of the synergy projects, a process that can be proved mutually beneficial to all parties involved. In this context, projects whose potential outcomes are related to those of RETENTION, and with which collaboration will be explored, are:

H2020 SC1-DTH-12-2020 funded projects (2 out of 7)

- **I-CARE4OLD** (https://cordis.europa.eu/project/id/965341) will develop and test next-generation decision support using high-quality internationally standardised routine care data, having a focus on predicting outcomes and the impact of treatments (from 52 million older recipients of home care and nursing home care from 8 countries) including reliable, valid and harmonised comprehensive assessments of functional capacities, diseases and treatments. This project aims to to improve prognoses and estimation of treatment impact for older care recipients with complex chronic conditions (CCC) in home care and nursing homes settings by developing, validating and testing individualised decision support.

Ties to RETENTION: a) Heart failure (HF) is a prominent chronic disease, b) exchange of knowledge regarding the performance of the HF-specific prediction models (model-driven big data analytics, c) cross checking and validating them against the clinical literature.

- **RE-SAMPLE** (https://cordis.europa.eu/project/id/965315) targets multi-morbid complex chronic conditions (CCCs) which is highly prevalent in patients with Chronic Obstructive Pulmonary Disease

(COPD). This project aims to introduce evidence-based, inclusive, preventive care and targeted treatment via predictive modelling through privacy-preserving Artificial Intelligence (AI).

Ties to RETENTION: a) the RETENTION platform will support clinical decision making and evidenced based personalised interventions for HF patients by continually monitoring and collecting several categories of data (including medical, clinical, physiological, behavioural, psychosocial) for HF patients, (b) analysing those using model-driven big data ML analytics, (c) detecting patterns in the HF disease progression and the quality of life of patients.

Other H2020 funded projects

- **BigMedilytics** (https://www.bigmedilytics.eu/) is the largest EU-funded initiative to transform the region's healthcare sector by using state-of-the-art big data technologies to achieve breakthrough productivity in the sector by reducing cost, improving patient outcomes and delivering better access to healthcare facilities simultaneously. The project is composed of 12 pilots that address three themes with the greatest impact on the sector—Population Health and Chronic Disease Management, Oncology and Industrialization of Healthcare Services— and covers the entire Healthcare Continuum from Prevention to Diagnosis, Treatment and Home Care.

Ties to RETENTION: a) increase productivity in the health sector by applying big data technologies to complex datasets while ensuring security and privacy of personal data.

- **IASIS** (https://project-iasis.eu/) goal is to utilise large, heterogeneous sets of data ranging from different sources, which if combined would enable the best decisions to be made, allowing for diagnosis and treatment to be personalised to each patient in two disease areas – lung cancer and Alzheimer's disease. IASIS is testing this approach in two disease areas – lung cancer and Alzheimer's disease – but with the longer-term ambition that this approach will be more widely applicable to other disease areas.

Ties to RETENTION: a) methods for combining information from personal medical records, and imaging databases to enable more personalised diagnosis and treatment approaches.

H2020 – FP7 Closed projects

- **HEARTEN H2020** (https://cordis.europa.eu/project/id/643694) developed an ICT co-operative environment that enable the HF patients to achieve sustainable behaviour change regarding their adherence and compliance, and the ecosystem actors to be engaged and improve the patients' HF management. HEARTEN targeted all actors related to the management of patients suffering from HF, including healthcare professionals, caregivers (formal/informal), healthcare providers nutritionists, fitness experts and health insurance experts, towards developing a multi-stakeholder patient centered mHealth ecosystem. The input data are complemented with nutrition information from the patient's smartphone, weight monitoring through wireless weight scales as well as the patient's profile and information directly added by the caregivers and the healthcare professionals. The multiparametric data are transmitted to the HEARTEN cloud architecture, where a knowledge management system analyses them and delivers critical information at hand.

Ties to RETENTION: a) RETENTION aims to take advantage of the Knowledge Management System based on artificial intelligence and data mining techniques that were developed within the framework of HEARTEN project, b) take into account presentation/interaction elements addressing the needs of all end-users categories.

- **SensorART FP7** (http://www.sensorart.eu/) project results include telemedicine services supporting patients with chronic heart failure (CHF) and healthcare professionals, allowing patients to be treated at home without renouncing to accessing high medical expertise. By monitoring the performance of cardiovascular implanted assist devices (VAD), patient's status and analyse the effects of heart and circulatory conditions along with the assistance conduction, the operation of these services aimed in reducing hospitalisation time, by considering also the higher degree of device acceptability at home by a training of the patient and his empowerment.

Ties to RETENTION: a) will consider the results of the Specialist's Decision Support Systems and the telemedicine features for CHF patients of SENSORART.

Relevant National and International Research Activities

- **ORCATECH Life Laboratory** (https://www.ohsu.edu/oregon-center-for-aging-and-technology/our-technology), a resource used to explore technologies to support independent living, to assess new behavioural markers, and to evaluate approaches for assessing neurological and other relevant health changes, all in the participant's home.
- **Microsoft Research Lab-of-Things** (https://lab-of-things.com/), a platform for experimental research that uses connected devices/sensors that makes predictive decisions about the home environment or resident's health status.
- **The European Society of Cardiology HF Long-Term Registry**, a prospective, observational registry which collects inpatient and outpatient HF epidemiological data from 21 European and/or Mediterranean countries.
- **SPHERE** (https://www.bristol.ac.uk/engineering/research/digital-health/research/sphere/), an interdisciplinary research collaboration (IRC) funded by the EPSRC and led by the University of Bristol together with the Universities of Southampton and Reading, aiming to gather information from multiple sensors around the home so as to monitor and track the signature movements of people in their homes and trigger a response in accordance with health needs.

Sensors utilised can gather and integrate various types of data about the home environment, including behaviours of home's residents to further understand a variety of healthcare needs.

- Outcomes of the **QUALIFY global survey** (124), that evaluated adherence to guideline-recommended therapies for HF.

2.5 Health Landscape Needs and Policies

Introduction

Hospital admission rates for Heart Failure (HF) have slightly decreased across EU countries (125). However, HF is increasingly prevalent in older segments of the population. With the proportion of elderly people rising rapidly, the number of cases is due to increase over the next decades. As the prevalence of HF grows, the economic pressure posed by HF on health care systems worldwide is increasing as well. Currently, it has been estimated that European countries are spending between 1-2% of their health care budget on HF (126). Due to the significant impact of HF on healthcare systems budgets, European countries need to implement

effective policies promoting better care for patients with HF as well as fostering innovation for the reduction of the costs.

This section presents a review of the state of the art of policies for HF in Europe and the current policy needs in the field.

2.5.1 Methodology and framework

This section adopted the methodology of a scoping literature review to identify the main policies targeting HF in Europe with a focus on five major European countries (France, Germany, Italy, Spain, and UK). Policies on the organization and structure of health care services in HF are often designed for different disease stages. To guide our review, we identify five main areas of the care and management of HF patients: (1) Prevention, (2) Primary care, (3) Secondary care, integrated model and palliative care, and (4) stakeholders' education. For each macro-area, three endpoints have been identified to ensure the comprehensiveness of the review, namely: (a) the policy landscape, (b) digitalization, and (c) policy needs. Peer reviewed and grey literature have been extracted for each endpoint.

2.5.2 Results

After three rounds of screening of both peer-reviewed and grey literature, 142 studies met the eligibility criteria of our research and were therefore included in the review. The included literature encompassed all disease stages, from prevention to end of life care. Sources from intergovernmental, regulatory and advocacy organisations were included in the screened body of evidence. The findings are presented below for each area of care.

2.5.2.1 Prevention

Policy Landscape

Prevention programs for HF encompass the management of wider lifestyle determinants of health, since cardiovascular diseases (CVDs) are correlated with behavioural risk factors, such as tobacco consumption, unhealthy diet, physical inactivity, and harmful use of alcohol (127). In Europe, all studied countries have in place advanced prevention plans. HF prevention policies are generally included in broader national policies targeting the prevention of chronic diseases. These policies may assume a disease-specific approach (128–130) or have a broader plan for the prevention of non-communicable diseases (NCDs) (131–133).

Examples of general policies are the Italian National Plan for Prevention 2020–2025 (134), the preventive act in Germany (135) and the new national strategy in Spain (136). The three plans focus on prevention of NCDs by strengthening health promotion in different settings, focusing on common risk factors, and reducing health inequalities. However, they take a disease-unspecific approach, with no mention of specific policies for cardiovascular diseases or HF prevention.

In England, Scotland and France, prevention policies targeting cardiovascular diseases have been developed by the respective governments. The Scottish government, in its "*heart disease: action plan*" (128), dedicates an entire section to prevention and reduction of risk factors of HF, proposing community prevention actions integrated with digital innovation using remote monitoring and applications (apps). The overall aim is to

reach a wider population and promote lifestyle changes. In France, “MA santé 2022” proposes prevention policies for cardiovascular diseases aiming to control risk factors and to promote changes in lifestyle habits.

An exception in this policy landscape of prevention is Poland. HF prevention policies were included in the Program for Treatment and Prevention of Cardiovascular Diseases – POLKARD (2017-2020). However, in the following programme for the period 2020-2025, there is no mention of specific actions for cardiovascular diseases.

Alongside broader national policy, a wider range of specific plans tackling specific lifestyle aspects indirectly connected to prevention of cardiovascular diseases, has been found in every study country. The plans tackle risk factors such as tobacco, obesity, and physical activity. Examples of these polices are the National Programme for Smoking Prevention and Tobacco Control (PNPCT) (137) and the National Program for the Promotion of Physical Activity (138), and the smoke free NHS agenda including milestones identified in the National Tobacco Control Delivery Plan (137). Other similar prevention programs specifically target the elderly population, such as the Long-term Senior Policy in Poland.

Another example of specific informal plans is the National Cardiovascular Disease Prevention System Leadership Forum (139) in England. This forum brings together government departments, arm’s length bodies, the NHS, professional organisations, academia, clinicians, and the voluntary sector to facilitate collaborative work towards shared objectives, with CVD prevention as the main goal.

At the European level, the European Heart Network (EHN) has been advocating for the improvement of prevention programs for heart diseases. Moreover, the HF Policy Network has been calling for a common plan for cardiovascular disease plan from the European Commission.

Digitalization

Prevention programmes and policies have been frequently paired with a wide range of digital technologies. These technologies offer health care systems the ability to track real-time vital lifestyle choices and disseminate health information to patients outside the hospital, therefore reaching segments of the population often excluded from traditional forms of care. As such, the European Society of Cardiology’s (ESC) CVD Risk Calculation App (127) provides healthcare professionals with calculators for primary and secondary prevention in various segments of the population.

In England, the NHS launched in 2015 the NHS Health Check, a national programme offering a health check-up for adults in England aged 40 to 74, repeated every five years (140). A similar initiative is the Heart Age Check, offered by the NHS online, aiming to raise awareness on behaviours that can affect the heart functionality (140).

Overall, the integration of digital technology, such as mobile apps, is increasingly becoming a key component of prevention policies and of raising awareness of healthy lifestyles.

Policy Needs

In recent years, CVD prevention has generally been promoted by governmental and scientific institutions, given its potential, if effectively implemented, in reducing hospitalization rates and the economic burden of HF (141). Different studies have proven that identifying the overall risk profile of patients would enable health professionals to plan effective long-term preventive actions. Therefore, providing continuous

implementation of prevention programs at all levels of care, actively identifying people at risk for heart diseases, continuously reducing and eliminating risk factors, changing lifestyles, and using therapeutic–pharmacological measures, will significantly reduce the morbidity and mortality rates from coronary heart disease. However, our review has identified an absence of a dedicated policy for the prevention of Heart Failure in Europe, highlighting a major policy need in this area (142).

Overall, countries are pushing for the digitalization of and innovation in disease prevention, however composite national plans combining prevention with digitalization are yet to be developed.

2.5.2.2 Primary care

Policy Landscape

The role of primary care in the management of HF is widely recognised as essential in the scientific literature (143). The gatekeeping and monitoring role of primary care providers often represents a first point of contact for people and allow coordinated care over time, particularly for patients with chronic conditions (143). Governments and scientific institutions have generally encouraged a shift from secondary to primary care and community-based management, recognizing its effectiveness in improving service delivery and patients' outcomes, by enhancing early diagnosis, providing ongoing support outside of the hospital, and reducing health expenditure (144).

Despite the recognized need for primary care policies supporting the delivery of effective care pathways, explicit policies targeting HF in the primary care setting are fragmented in Europe and have been identified only in few countries (Italy, England, Scotland, France). In Spain and Germany, only policy proposals have been identified. In 2020, the Spanish government launched a strategy with the overall objective of improving care and outcomes for patients with CVDs and their families(136). The strategy emphasises the improvement of cardiovascular care through the development of integrated, participatory, intersectoral and continuous care that guarantees better socio-health coordination, and reduces the inequalities caused by gender, socioeconomic status, and functional diversity. However, the government has not implemented a concrete strategy yet. In 2021, in Germany, The Institute for Quality and Efficiency in Health Care (IQWiG), on behalf of the Federal Joint Committee (G-BA), has called for a revision and improvement of care aspects of the current programs dedicated to Chronic Heart Failure but still no formal policy has been implemented (132).

France, England and Italy have been including policies targeting primary care organization in HF management. In France, "MA santé 2022" identified detection, screening, and management of early chronic pathologies as key areas of improvement, highlighting the need for strengthening and formalising the HF care pathway. (145)

In England, the NHS long term plan (139) dedicates an entire section to the improvement of primary care in HF, pledging to support early diagnosis by enhancing health records screening and improving access to screening devices.

In Italy, specific HF policies in primary care have been developed as part of the National Plan for Chronic Conditions (Piano Nazionale della Cronicità), in which a strategy for the improvement of HF management and care in primary settings was proposed (146).

In Scotland, an entire section of the "*heart disease: action plan*" (128) has been dedicated to the improvement of pathways for the diagnosis and treatment of cardiovascular disease, with the overall aim to introduce a set of homogeneous pathways for the entire country. Specifically, Scotland proposes community care models aiming to reach population segments less likely to engage with the health care system, and to promote the development of tailored-made local provisions to address health inequalities.

At the European level, the European Society of Cardiology (ESC) provides diagnosis and management guidelines for primary care which are endorsed by several European cardiology societies and are revised every five years (147).

Beyond primary care policies, our review revealed fragmented policies in the screening for HF. One of the main goals of primary care policies is to detect HF cases in the early stages of the disease, and to identify high risk patients (148). Screening activities are therefore considered essential for the early diagnosis of HF and for the identification of high-risk patients (149). In recent years, risk stratification has been widely improving owing to the use of biomarkers and statistical models ranging from risk scores to clinical decision support systems (CDSS) based on algorithms and/or artificial intelligence tools(150,151). Determining the overall risk of heart diseases opens the way for healthcare providers to accurately plan a preventive strategy, including dietary and physical activity advice, pharmaceutical treatments and regimens' options and monitoring needs (142). This, however, has not always been incorporated in policy actions. For instance, the reimbursement of diagnostic tests, such as the natriuretic peptide (NP) testing, is adopted at primary care level in some countries only (France, Germany, Italy). This type of testing allows the early identification of HF cases and prevents bottlenecks around access to echocardiography (148). These innovative analytics are fostering the implementation of precision medicine principles in HF care, which aim to tailor treatments and predict health outcomes at individual level. Advanced analytics can predict, for example, individual responses to cardiac resynchronization therapies (CRT) at an individual level (152). Improving diagnostics is explicitly mentioned in the Scottish "*heart disease: action plan*" (128), the Belgian Charter for Heart Failure and the Spanish Society of Cardiology (153), specifically calling for improving the reimbursement of PN tests, which are not always reimbursed in these countries. The Belgian Charter for Heart Failure, specifically, lists the reimbursement for recommended diagnostics as one of the five priorities for political action (143). The Spanish Society of Cardiology published quality standards for integrated diagnosis by specialists and accreditation for IC units. These bring together the diagnosis, treatment, and clinical follow-up of patients with HF based on the guidelines of clinical practice and establish minimum standards of coordination with primary care. The program recommends a PN test in primary care if a possible case of HF is suspected (144).

In Scotland, the policy places emphasis on the importance of supporting the development of pilot projects of innovative care models for cardiac diagnostics, thus allowing to learn from and scale up such models to ensure that everyone across Scotland can benefit.

A number of initiatives to promote better HF management in primary care settings have been developed at local level. In the United Kingdom, the One Simple Blood Test campaign launched by the Pumping Marvellous Foundation raised awareness among general practitioners on the use of natriuretic peptides testing to facilitate earlier diagnosis of heart failure (154). In Catalonia, the Bellvitge University Hospital and Catalan health service implemented a pilot program for HF management program coordinated by nursing staff in primary care(155). Since 2019, in Poland, the HF working group of the Polish Heart Society, the Ministry of Health and other primary care associations are applying new models of multidisciplinary clinical management

for HF care in five local hospitals. The overall objective of the project is to improve the understanding of patients' needs and to develop reimbursement policies for the long-term care of HF (156).

Digitalization

Cardiologists have been integrating basic forms of digital health into their practice for decades, from telephone consultations to electronic health records (EHRs). In the last decades, the new advancement in digital health brought the introduction of new technologies in the traditional model of heart failure (HF) outpatient care, such as remote monitoring (RM), teleconsultation and electronic patients records (157).

The development of electronic patient records and shared data has been one of the main targets of policies aiming at the digitalization of primary care. Countries have been focusing on the improvement of electronic patient records to enhance the exchange of vital information in the primary care setting. For example, Denmark has shown notable improvements in primary care quality, by including, in their electronic patient records, data on diagnoses, procedures, prescribed drugs, and laboratory results and by enabling the system to automatically derive information that can be used to benchmark GP practice against other practices, and to improve patient care by identifying patients treated sub optimally (143).

In England, the NHS Long Term Plan dedicates an entire program, CVDPREVENT to improve national primary care audit. The program routinely extracts GP data covering diagnosis and management of six high risk conditions that cause cardiovascular diseases, providing a pathway to improve GP practices' use of data. By creating Primary Care Networks (PCNs), CVDPREVENT supports better understanding of the number of patients with CVD and/or high-risk conditions that are potentially undiagnosed, or under or over treated. Therefore, the audit will provide a double service: 1) improving and monitoring diagnosis and management, and 2) identifying gaps, inequalities, and opportunities for improvement (139).

In Italy, the Pact for Digital Health, launched in 2016, promotes the dissemination of digital health care (eHealth) in a coordinated way across the country, highlighting the need for enhancing the current system of electronic patients' records. The main priorities of the program were the development of patients' electronic records, telemedicine systems and innovations in the information communication technology (ICT) sector, potentially improving the workflow management and patient treatment. The pact was followed by the digital growth strategy and the three-year plan for public information technology administration (2019-2021). However, this has not targeted specific HF needs (146).

Our review found a growing number of policy initiatives focused on the improvement of telemonitoring. In England, Self-tracking apps, text messaging and remote self-monitors have the potential to connect with a wider population, and thus improve the NHS' ability to identify people with high cardiovascular risk and improve lifestyle management interventions. (139).

In Scotland, Heart Failure Remote Health Pathway promotes a collaborative approach between clinicians, digital technicians, patients and third sector organisations to develop a remote monitoring pathway specifically for people with newly diagnosed heart failure or unstable symptoms, enabling clinicians to remotely monitor a patient's blood pressure, heart rate, bodyweight (in some cases oxygen saturation) and to answer several health-related questions. This is combined with the development of indicators and improved data collection for all three conditions (high blood pressure, high cholesterol, and atrial fibrillation)

can support local quality improvement within primary care and make data available at regional and national level to identify unwarranted variation (128).

In Germany, the G-BA recently decided in favour of reimbursing the costs of telemonitoring for advanced heart failure, by the statutory health insurance, as an outpatient service. However, the recommendation of a proper monitoring service offered by the German NHS is still lacking in the disease management plan.

Policy Needs

In the recent years, a shift from secondary to primary care of HF patients has generally been encouraged by governmental and scientific institutions because, if effectively organised, it would improve patient outcomes, enhance early diagnosis, provide ongoing support outside of the hospital, and reduce health expenditure (Health Failure Policy Network, Alliance for Heart Disease). A routine healthcare study reported how there's a correlation between stronger primary care and lower levels of hospitalising among elderly multi-morbid patients, and particularly among the high-risk ones. In particular, the study evidence how, compared to different diseases, long-term benefit of primary care is greatest, among patients with CHF and chronic heart diseases, in reducing hospitalisation (141).

However, advanced analytics and precision medicine principles can be effectively implemented in HF care if many challenges are addressed by the health system, related to granular data availability, effective monitoring, effective use of electronic health record (EHR) and targeted integration of different tools and therapies(141).

HF primary care is generally based on the adoption, at country level, of national guidelines and local care pathways, such as clinical pathways for general practitioners (GPs) and cardiologists, cardiac rehabilitation and palliative care programmes (Denmark, Portugal) , and therapeutic education guidance (France) (130) Furthermore, different European countries have set national guidelines related to HF. In the United Kingdom, where more than 900,000 people are affected by HF, the National Institute for Health and Care Excellence (NICE) issued a set of diagnosis and management guidelines for adults (158). Germany issued clinical recommendations for healthcare professionals (159). While Italy and France released guidelines on standard of HF care(130,160,161). However, different challenges in applying primary care guidelines in healthcare practice persist. In a UK study involving 39,301 patients with HF from 359 GP surgeries, monitored for 4 years, it emerged that, while 90% of patients used health services, the use of GP consultations and community rehabilitation services were considered low and inadequate by the authors (158).

Secondary care, integrated care models and palliative care

Policy landscape

People who are hospitalised due to HF require appropriate after-care to ensure that chronic heart failure does not develop. This includes self-management, remote monitoring, and timely interventions, as needed. The literature suggests that an integrated model of care for heart failure, organized within a heart failure specialized clinic, can improve patient's survival and quality of life while reducing hospital admissions. In an integrated care model of care for HF patients, multi-disciplinary teams (MDT) are considered an essential component. MDT aims to foster integration of care across health professionals. Teams usually include nurses, doctors, pharmacists and dieticians. This approach can lead to better health outcomes for patients, improve

care coordination across services and organisations, and lead to reduction in costs, primarily through reducing hospital admissions (162).

Different programs of integrated care pathways for chronic diseases and specifically for heart failure have been proposed in Europe. National policies, however, have been scattered with mostly calls for action and local initiatives fostering innovation in this segment of care.

Since 2017, the Polish government has implemented a new complex care model for acute myocardial infarction (AMI) patients based on the European Society of Cardiology (ESC) guidelines (163). The model aims to improve secondary prevention measures, quality of care and long- term health outcomes in AMI patients and it represents the first nation-wide model of structured and comprehensive post-AMI care (163).

In France, improving care for patients with NCDs is one of the priorities set out in the 2018-2022 regional health project as well as in the Health Reform Law. Both documents are proposing multidisciplinary working models allowing a shift from hospital to community settings through strong coordination between all the stakeholders.

At local level, Paris' local authority (the ARS Île-de-France) launched in 2019, pathways for patients with chronic heart failure, and organized regional events in partnership with the health Insurance.

In Germany, in 2018 a national Disease Management Programme (DMP) for HF was introduced with the goal of enhancing patients' quality of life and reducing the overall burden of HF on people and healthcare systems by reducing hospitalization and improving the management of comorbidities. Recently, IQWIG - the German independent institute for quality and efficiency in health care -pledged for an improvement of CVDs guidelines, mentioning specifically the importance of implementing better integrated care models (132).

In Italy, the Pact for Health recognises the importance of reducing hospitalisations and improving quality of life for people living with HF, and, among other objectives, it explicitly states the need for developing MDT for the care of HF patients. Italian professional societies and non-governmental organizations developed a comprehensive guidance framework promoting multidisciplinary and integrated HF care and published various joint consensus documents to promote best practice in HF care (164).

In Spain, different healthcare associations published a consensus document aiming to improve outpatient HF care through better integration. The document proposed the development of a national HF network of healthcare professionals working at three different levels of care: community HF clinics, hospital HF clinics and advanced HF clinics. The network aims to integrate in-hospital and outpatient care with other healthcare professionals, such as GPs and social care workers, to ensure a seamless continuity of care. It is unclear, however, whether the implementation of this pathway for outpatient HF management has been initiated. Moreover, integrated care models are not homogenously implemented at national level, but they have been promoted in an ad hoc fashion in hospital and universities. For instance, the health care institutions in the Litoral Mar area and the Catalan Service of Health developed a multidisciplinary model for HF care coordinated by nursing staff, which reduced the risk of readmission and death (133).

In the UK, the NHS Long Term Plan explicitly recommends the improvement of HF management by expanding multidisciplinary HF teams in primary care and increasing access to cardiac rehabilitation and HF specialist nurses in hospital settings. The MDT approach is also emphasized by NICE guidelines (165). However, an analysis of Northwest London primary and secondary care activities revealed low frequencies of GP

appointments and low levels of cardiac rehabilitation, therefore suggesting a lack of adherence to the MDT approach (165).

End of life care has been frequently overlooked in the secondary care of HF. However, it has increasingly become relevant in HF management. The UK National Palliative and End of Life Partnership set a framework with 6 objectives for HF patients end of life care (166). The overarching principle of the framework is that care should be tailored to everyone, through specific coordination and review among health professionals. Despite the plethora of guidance documents published on the subject by the English NHS and Department of Health, the health system is still far from fully implementing the Advanced Care Planning (ACP) principles: late decisions and diagnoses often lead to deaths in acute hospital beds, therefore not allowing patients to stay in their preferred place of care. Old approaches, such as delegating end-of-life care to primary care, persist and limit the application of ACP principles (166). Palliative care programmes have been proposed by some countries (Denmark, Portugal, and Scotland); however, the extent of their implementation is yet to be seen.

Few practical initiatives have been developed to promote policies in HF palliative care. In England, the British Heart Society (BHS) has been advocating for the recognition of national strategies and guidelines on palliative care provision for all chronic life-limiting illnesses comprising HF. Italy developed detailed guidelines to include palliative care in the HF disease management, and different associations (131).

Digitalization

Digitalization strategies and policies in secondary care settings and integrated care models have been mainly focusing on policies connecting different healthcare professionals and organisational levels (e.g., hospitals with GP practices), improving IT infrastructure in hospitals and enhancing the integration between traditional pathways of care and innovative digital tools.

In all the countries of study, Digital Health strategy for the improvement of the IT infrastructure at national level have been implemented, however these are not directed to HF specifically. For instance, In Germany, the Digital Care Act (2019)(167) and the Hospital future act (2020)(168) fosters the introduction of digital technologies across all care settings. Specifically, the Digital Health Care Act defines and strengthens the reimbursement criteria of health apps prescribed by healthcare professionals under public health insurance whereas the Hospital Future Act aims to improve the IT infrastructure in hospital setting, promoting a cross-sectoral telemedical network structure.

Our review identified HF-specific digital strategies in integrated care in Spain and France only.

In France, policies regarding digitalization of the national health system are included in their “Ma santé 2022” strategy under a dedicated action called “E- parcours”. The action has two aims: firstly, to transform healthcare pathways by providing a range of digital coordination services for the health and social care sectors, making use of basic services such as shared medical files, thus decompartmentalizing care; and secondly, to connect Hospitals with GP practices by developing an interconnected Hospital Information Systems (HIS) to ensure the continuity of healthcare pathways between hospital and GP providers. .

In Spain, a collaboration between hospitals, CardioRed1, has recently implemented a monitoring program for patients with heart failure (HF) combining face-to-face and telematic consultations (169).

Policy needs

In the development of integrated care model, our review found that there are still wide policy needs and barriers. Firstly, despite the proposal from many countries to introduce integrated care models between primary and secondary care settings, there is still fragmentation in policy actions in Europe. Clear policies should be designed aiming to integrate different level of care, fostering communication, and date sharing across healthcare professionals and combining innovative digital health technologies with care pathways.

Secondly, even when integrated pathways have been set, studies revealed an overall lack of adherence by providers and patients. i.e. lack of or poor diagnosis and low patients' awareness and health literacy.

Thirdly, the implementation of digital health tools aiming to help the integration of primary and secondary care is still hampered by lack of digital skills among the workforce as well as lack of integrated and compatible IT systems. Frequently, the health care infrastructures are not suitable for the introduction of new digital technologies. Our review identified that there is a current need of polices enhancing the interoperability across digital technologies and settings. For instance, electronic health records (EHRs) are routinely implemented in European countries in primary care setting, however they are often not designed to extract and share data with secondary care specialist. Therefore, there is a need to design policies to implement appropriate IT infrastructures that allow the introduction of innovative devices and wearables(170).

Fourthly, coordinating HF care represents a challenge for all the involved stakeholders, from patients to families, caregivers, health providers and health and social care economies (162). There is no standard guidance regarding the actors/stakeholders who should be specifically involved and the goals that should be achieved, leaving it up to local care units to organise their MDT and care pathways (158).

Finally, end of life care is currently a major challenge related to secondary care of HF. In most study countries, no policy or strategy to introduce palliative care into the management of HF has been identified, highlighting an unmet need in the area.

Stakeholders Education and Coordination

Policy landscape

Health professionals

In 2021, the European Health Management Association (EHMA) and Health First Europe (HFE) published a joint statement on the profile and training of future healthcare workers, calling for specialized educational programs and integrated approaches for care. Providers' education in HF is recognised as an essential component for the improvement of health outcomes for HF patients (148). Setting dedicated training programmes on HF management and specific educational methods and topics are proposed as solutions to the lack of healthcare professionals in the literature (171).

Policies for the education and coordination of providers have been promoted across European countries with formal accreditation offered in England, Scotland, Germany, and France. England has been at the forefront of training in HF with the first accreditation programme launched in 2002. Currently, NHS England offers a wide range of services with specialist nurses, trained in HF, managing the services, although clinical expertise varies greatly.

In Scotland, HF patients are supported by HF specialist nurses. Many rapid access chest pain clinic services are nurse-led, and a genetic testing service for hypertrophic cardiomyopathy (HCM) is supported by specialist nurses. In addition, in its "*heart disease: action plan*", the government developed a Recovery and Rehabilitation Framework plan to advance health professionals' education and coordination, promote collaborative work models, and ensure the correct training for health professionals in specific CVDs areas.

In France, in December 2019, the Ministry of Social Affairs and Health developed a pathway for providing nurses with the relevant training to manage HF patients.

In Germany, HF specialist nurses receive a formal accreditation, and continuing medical education in HF is provided to cardiologists by the German Cardiac Society.

In Spain, health associations have promoted healthcare workforce training. For instance, the Spanish Society of Internal Medicine (Sociedad Española de Medicina Interna, SEMI) offers training on diagnostic tests and management of HF and the Spanish Society of Cardiology Sociedad Española de Cardiología, SEC) has a well-known accreditation programme (SEC-EXCELENTE) for HF units in cardiology departments.

In Italy, AIFA promotes a major collaboration and communication between all the stakeholders (i.e. research centres, patients and physicians associations, regulators, payers and pharmaceutical companies) to address unmet needs and poor HF management (172). Also, professional and advocacy organisation can directly help in improving awareness and in educating physicians and other relevant healthcare professionals, since they have a large membership and communication networks in many countries (173).

Patients

Patients' awareness of the disease and good levels of health literacy emerge from the literature as two relevant factors impacting HF management and health outcomes. Awareness and education are fundamental to help patients in self-managing their disease.

Different programs have been developed for self-management education in the context of HF, such as telephone education support, disease management clinics, telemonitoring, nurse and multimedia-based education, and combinations of telemonitoring and telephone support (171). Self-management helps patients in understanding how to react to HD symptoms, increases self-confidence and can improve quality of life of patients with HF (171).Also, education and awareness can be decisive in managing specific stages of the disease such as the hospital discharge, which is considered the most vulnerable period for patients as low levels of engagement after discharge are recorded (174). To ensure patient engagement, other practices have been suggested, such as direct liaison with health professionals via calls, or via automated short text messaging and digital tools. Another proposal to improve patient engagement includes family involvement in healthcare practice though family advisory councils (175).

Health literacy is directly correlated to quality of life of HF patients and is a significant predictor of self-care behaviours in older patients (176). Health literacy can also enhance the use of advanced care planning (ACP), which aims at promoting a "voluntary process of discussion about future care between an individual and their care providers, irrespective of discipline"(166). This would allow patients to better report their concern and preferences on the disease management and on treatment options (166).

In Spain, two government funded programs, ITERA and PRISMA, made available a series of tools to help people coexist with the HF. The tools include: a guide that explains what HF is, its symptoms, causes and possible treatments; a table to control the medication; a guide with detailed dietary recommendations; a guide to recommended exercises; and a table to record weight measurements; and support in determining the need to contact a health professional. The program has facilitated the development of HF units in Spain, and preliminary results showed an improvement in self-care, functional ability, and quality of life.

In Italy, the Italian Association of Heart Failure Patients (Associazione Italiana Scompensati Cardiaci) has developed a program to support people living with HF and to raise awareness among the public. The association distributes educational material in meetings and offers on-site specialist visits.

At European level, different awareness campaigns, such as the European Heart Failure Awareness Week, have been implemented to raise patients' awareness.

Digitalization

Digitalization has not played a key role in HF providers or patients' education yet. Our review has not identified any programs fostering the education in digital health technologies in HF for healthcare professionals nor patients and only digital app pathway raising awareness on HF management across Europe. In Italy, Italian Association of Heart Failure Patients (Associazione Italiana Scompensati Cardiaci) has launched an app aiming to raise awareness among patients on care pathways and risk factors in HF.

Policy needs

When considering education in HF, policy needs have been identified in three main areas: (1) formal education programs and accreditation for healthcare professionals specialized in HF (2) digital education of healthcare workforce (3) patients' digital education and awareness.

Currently policies on accreditation programs are growing in European countries. However, there is still a policy gap in the HF training which is mostly conducted by primary health care associations and specialized centres. Formal education pathways should be developed at national level and integrated with traditional medical education curricula. Formal accreditation of HF specialism, which is considered crucial for long-term management and positive outcomes, can expand specialist workforce and therefore enhance professionals' education and awareness on HF management (144).

Our review found that overall improving digital health literacy among health care professional through targeted programs is a policy need in this area. The body of included evidence looks at education of health care professionals in digital health as a main challenge. If recent innovations brought by digital health can help healthcare professionals in following patients, many of them perceive reviewing data and providing feedbacks based on supplementary digital tools as time consuming tasks (177). This perception is also caused by the fact that many digital tools are still used on top of existing care, and therefore are not fully integrated in clinical practice. Barriers for physicians in the use of digital health are generally related to lack of clear regulation and standardisation, poor digital infrastructure, absence of incentives and access to knowledge and training programmes (177). There is therefore a need of implementing education and capacity-building programs for health care professionals.

Finally, our review found that patient digital education poses still a challenge for European countries. Reaching higher levels of health digital literacy represents a challenge as HF mainly affects older segments of the population, who tend to be less willing/able to learn new concepts and to use new tools (123). From the literature, it emerges that older populations have generally reported lower levels of acceptance of the use of smartphones (123). Furthermore, a high prevalence of inadequate digital health literacy in older patients has been reported in developed countries like United States and South Korea (176). Overall, self-care challenges are related to knowledge gaps, recognition of health deterioration, poor self-motivation, and limited knowledge of appropriate action plans. To monitor and assess patients' experience and behaviour, patient-reported outcome measures (PROM) are increasingly utilised. These measures could also enhance patient-clinical interaction, patient-centred care and shared decision making on treatments options(178).

Conclusions

Nowadays, HF is becoming increasingly a challenge for health care systems, with 26 million individuals living with the diseases globally (179). HF affects every level of the health care system and the current overall HF policy landscape in Europe is fragmented with most actions being included in wider policies focusing on the prevention and management of chronic diseases. There are few examples of well-designed policies implemented at local level or call for policy actions from professional and patients associations to improve HF prevention and management, however they often do not seem to be followed by national-wide policies.

Overall, our review found that prevention and early diagnosis of heart failure patients, as well as shifting care to primary settings should be one of the priorities in national policies. Another priority is the reduction of hospitalisation and re-admission of HF patients which can only be achieved through integrated models of care that include multidisciplinary teams connected through robust electronic health records and data sharing across care levels, coupled with user friendly digital/remote monitoring that empowers the patient to self-manage his condition and allows for timely and specific interventions.

Based on this, RETENTION proposes the development and assessment of a robust and comprehensive platform able to collect and analyse clinical, behavioural and real-world patient data, in order to develop personalised care decisions and interventions with the objective of reducing hospitalisation and improve patients' quality of life.

3 RETENTION User requirements

3.1 RETENTION ecosystem

There are three main actors or users of the RETENTION platform:

1. The patients. There are the main actors of the platfom. Three types of patients will be included: heart failure (HF), left ventricular assist devices (LVAD) and heart transplant (HT) carriers. The platform is meant to empower them in the management of their disease.
2. Informal caregivers. There are also an important part of the disease management for most of these patients, since they will support them and facilitate their daily routine with the provided technological system.
3. The clinical team (HF doctors) responsible for surveillance of clinical parameters, follow-up, and treatment.

In addition, the following secondary users have been identified.

1. Public health experts: they will be able to access to RETENTION data to plan and evaluate public policies related to HF patients
2. Data scientists/Researchers: They will be able to access to RETENTION platform to analyse and identify new HF landmarks
3. Hospital IT /admin teams

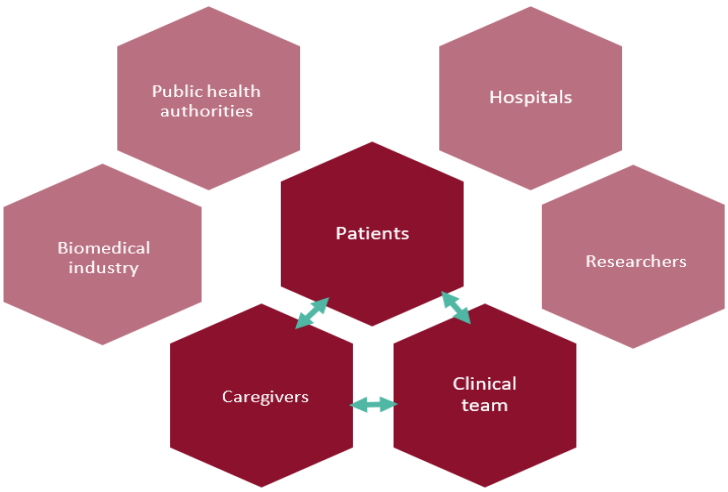

Figure 8. RETENTION ecosystem with users presented in dark red and secondary users in light red.

3.2 User requirements elicitation methodology

The main objective of Tasks 3.1 & 3.2 is to provide a precise description of the content, functionality and quality expected by the RETENTION platform perspective users. For the purposes pf D3.1 the application of different user requirement methods is based on a four-step process including: (1) research process and state of the art about the topic, (2) User needs identification: questionnaires and interviews for different actors (3) Re-evaluation, (4) requirements specification (as it is shown in figure below).

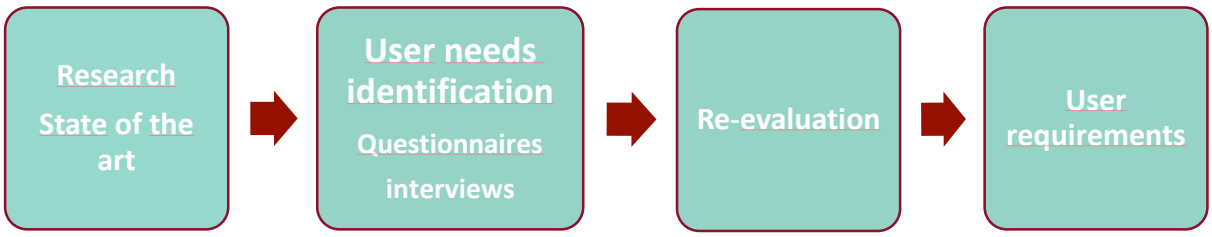

Figure 9. Process for user requirement analysis

The first step in this process was to conduct research, collect information about the users and stakeholders according to the current clinical practice and compose the most current state of the art about telemonitoring in HF from a clinical perspective (and technologically solutions (as well as from the current regulations and policies point of view. Results of this research process are provided in section 2 of the deliverable. The information gathered during this step was the basis for the preparation of questionnaires presented in Appendix 9.1 (a consent form was also prepared for the questionnaires). Once the necessary information has been collected and the users have been identified, user needs identification can be achieved through the utilization of questionnaires, focus groups, interviewing and use cases. Specifically, after the reviewing of the questionnaires by all the consortium members, they were circulated by the clinical experts of the consortium to the users. Patients and carers questionnaires were translated and distributed in each of the participants institutions. Clinicians (also providing information for the researcher type of user) were contacted by email to answer the questionnaires through a google form questionnaire link. In addition, through physical or virtual meetings an interview with 5 IT representatives (one from each clinical partner) was performed.

The next step, the re-evaluation, refers to the existing developed system that can be achieved by brainstorming and usage scenarios or a combination of them. Finally, the last step, user requirements, where for each requirement, (i) identification of the relevant users and secondary users, (ii) a clear statement of design goals, (iii) the priority level, (iv) the means of verification, (v) the acknowledgement of legislative requirements should be documented. An explanation and a comparison summary of the methods that can be applied in each step of user requirement elicitation process are provided in (180). Through this user centric approach, RETENTIONS ensures the active involvement of the users from the early design phase. Workshops done during the next project phases will keep on involving users in the development of the project.

3.3 Questionnaires and interview results

The overall achieved number of questionnaires acquired from the 5 participant clinical centres were 163. Specifically, it was estimated that the consortium partners provided 74 questionnaires for patients, 55 questionnaires for caregivers and 34 for clinicians. In the beginning of each questionnaire there is a consent form provided to the users. The following table summarises the questionnaires collected per user type and institution.

Table 2. Number of questionnaires

	Final number of questionnaires
Patients	
SERMAS	17
UK ESSEN	10
UNIBO	13
OCSC	14
NKUA	10
TOTAL 1	74
Caregivers	
SERMAS	14
UK ESSEN	6
UNIBO	10
OCSC	15
NKUA	10
TOTAL 2	55
Clinicians	
SERMAS	9
UK ESSEN	5
UNIBO	9

	Final number of questionnaires
OCSC	6
NKUA	5
TOTAL 3	34
GRAND TOTAL	163

To be aware of the potential technical barriers in the implementation of the RETENTION platform, an interview with the responsible person of the IT department in each of the 5 participant hospitals was performed. Questionnaire answers are included in the Appendix 9.2. The results of the questionnaires and interviews are analysed in detail in the following sub-sections.

3.3.1 Patients

Most patients are 40-70 years, graduated from high school, retired, suffering from HF, and mainly men (2/3). Almost half of them have a smartphone that costs less than 200 euros and 1/3 over this. Over 80% have a PC, an internet connection, and relevant skills. This percentage falls to 60% concerning the use of apps generally or specifically in health. 2/3 of these patients would frequently use a mobile app or web application for their health, or/and have already used a digital health device, or/and will be willing to wear such a device. 2/3 of these prefer a smart phone compared to those (1/4) who prefer a tablet (1/10 none). 2/3 of patients prefer to have a chat with a clinician or/and a reminder for check-up, visits, and medications, as well as alerts to a doctor in emergency cases, while half of them agree to be measured daily for relevant to their disease or health activities.

Almost half of them prefer to be educated from short videos and almost 40% from written notes. Most of the patients accepted to answer a quality-of-life questionnaire, even per month. However only 1/3 of the patients accept to spend time per day on such a platform to monitor their health, and over 80% are not willing to maintain such information in the platform. On a contrary over 80% of the patients, suggest the connection of the platform with their hospital files. That's why over 80% would need help from e. g. a caregiver or companion to use the platform. Finally, 80% of the patients accept to manually insert 4-8 parameters in the platform. And over 80% accept only their doctors to give alerts if these parameters been detected.

3.3.2 Caregivers

Most of the informal caregivers are below 60 years. 25% have finished grammar school, 35% high school and 40% colleges and universities at any level. They are mainly women (80%). Over half of them have a smartphone that costs more than 200 euros and over 1/3 less than this (the others have a non-smart phone or nothing), on a contrary to patients, as it has presented above. Over 80% have a PC, over 95% an internet connection, and 80% relevant skills. This percentage falls to 60% concerning the use of apps generally or specifically in health. Over 2/3 of them are husbands or wives related with patients. 11% are sons or

daughters, another 11% other relatives and only 9 % professional caregivers. They spend 1 hour (1/5), 1-4 hours (1/5), 4-8 hours (1/5) or even full day (1/5) to their patients, mainly for medication etc.

Over 2/3 of informal carers would be willing to provide patient data to the mobile app. Half of them said that their patients can use a web application for their health or/and a digital health device, and the other half that their patients need some help, mainly meaning from them. Over 2/3 of these carers prefer to have a chat with a clinician or/and a reminder for check-up, visits, and medications, as well as alerts to a doctor in emergency cases, all for their patients, while half of them agree to be educated for their patient's disease or health activities. Over 2/3 of them will be willing to such a device for their patients. Half of them prefer to be educated from short videos and the other half from written notes. Most of the carers accepted to answer a quality-of-life questionnaire, even per month, for their patients. Most of them accept to spend time per day on such a platform under doctors' instructions to monitor their patients' health. And over 85% would like to receive warnings and recommendations from their patients' doctors.

3.3.3 Clinicians

Doctors responded are 25-50 years old. Most of them have 5-15 years' experience. They have treated 97% heart failure (HF) patients, 47% LVAD patients and 56% patients for heart transplantation. Most of them do not have experiences with remote monitoring in HF patients. However, their majority think that a designed app will improve their patients' conditions. Most of them or their teams use remote cardiac implant devices (ICD), indicating apps (m heart, customized, telemedicine, sensors, etc.).

Concerning a design of requirements for patient edge gateway, 60% of doctors would skip in-person visits with a telephone call or video chat, 70% of doctors would prefer protocols within the platform, many of them consider useful for their patients to have chats with other clinicians and reminders for their patient's medication and visits, while they need statistics, educational materials, etc.

Concerning a design of requirements for clinical site backend, patients' weight, their blood pressure and heart rate, ECG, fluid balance, etc. are most useful for the doctors responded, 85% of the doctors need patients' clinical data to be available on the platform, a little below 80% would like to receive warnings for their patients' health status, indicating the main reasons of these warnings (high heart rate, rapid weight increase, high blood pressure, desaturation, and other symptoms), the best way to receive notifications is mainly through an app and then emails and platform, they prefer to consult patient data through apps and PC programs, they see patients' data daily or weekly, and less than half are familiar to AI.

Doctors' proposals for the retention in the clinical setting show that almost 75% consider the platform useful, with limitations in their time and generally the cost, they indicate patients' difficulties as the main barrier, and finally, they have ethical considerations e.g., system safety, use of data, etc.

3.3.4. IT Managers

Concerning Technical Requirements, the IT managers of the 5 participating hospitals concluded in the following:

- There is an availability of a complete and accurate Electronic Patient Record and appropriate Information Systems to accommodate and support it.
- There is complete and accurate historical data in adequate for at least from the last decade to maximum the previous ones.

- RETENTION system can be connected to the HIS/ERP or other hospital system, by using HL7. Still, during the pilot phase of the RETENTION project, connection with the hospital information systems/EHR is not possible due to security policies.
- There is a compliance with EPR standards (e.g., HL7 and others), so that data can be interchanged between medical facilities, considering the above answer(s) too.
- They agree reaching an agreement on the exact technical specs (both functional and non-functional), of the platform, from the various user groups and project stakeholders, however they suggest meetings with technical contributors or technical staff assistance through Retention project or relative approvals (SERMAS) etc.

Concerning Barriers, the IT managers of Hospitals of partners of the Retention replied:

- There is no reluctance or ignorance of the high management to the project.
- There is no reluctance of medical staff (doctors) to get involved in the project due to the lack of time (especially in the times of the pandemic), especially doctors, who are engaged to the RETENTION, have strongly motivated.
- Many of them have experienced technical personnel for (1) development & use of modern software tools and (2) data processing skills combined with appropriate clinical knowledge. Some of them need experienced and available staff and it was indicated to the specific retention leader to examine it.
- The most important issue is additional data required from patients, and the follow up of them might not so regular. So, it is sometimes difficult to get in touch with them, but it must be solved, concerning RETENTION, through the questionnaires, etc.
- It is difficult to estimate, any cost for the above, because it depends on many factors. However, the costs might not be a severe issue, because most of the required infrastructure already exists in the framework of the normal hospital operation. Working costs, in most cases, could be covered within the project (retention) budget.

Conclusion

Patients like the idea of having a mobile device with an application that will be able to keep them in the right track, by providing reminders for their pills, fast connection to their doctors and hence connection to the medical institution, and enhanced data acquiring capabilities, so they can readily and easily transmit to their doctor and finally in an emergency to be able to connect to the doctor. The patients are willing to have a minimum set of data to pass to the RETENTION system and prefer the carer to do the rest of the data collecting and passing to the system. Their carers on the other had are willing to insert data into the RETENTION system, are willing to talk to the doctor and other personnel to have immediate help if their loved one is incapacitated, have the system remind them and the patient about taking the treatment, and have the system as a support. Both patient and carer would like short notes or videos on treatments and other HF remedies, with minimal loss of time. Also, would like to have the appointments to be made with the RETENTION Platform. As for questionnaires, they mostly agree that it should done in a periodic model 15 to 30 days.

Clinicians' opinion is that a system like RETENTION will be beneficial for their patients, by keeping the adherence to treatment, keep a tap on basic and if need be advanced indicators. Chat (audio or video) is recommended, especially on emergency situations. All patient indicators should be checked once a week at least and special warning should be given by the system at emergency situations. They are not familiar with

AI tools but would like to see them on a clinical trial. Finally, the clinicians believe that their patients will have different barriers to work with the system.

IT managers stated in their hospitals, accurate and detailed electronic health Records exists for patients. The Hospital systems can be technically integrated with the RETENTION system. Still, during the pilot phase of the RETENTION project, connection with the hospital information systems/EHR is not possible due to security policies. This can be done after the project pilot implementation under specific terms and agreements.

4 Clinical study characteristics - Risk factors and technology solutions

According to the questionnaires' results, the patients and caregivers would like a telemonitoring system that:

- Focuses on the patient
- Allows a fluid communication with clinicians
- Allows clinicians and caregivers participating in the RETENTION system
- Integrates all the cardiovascular care aspects (from educational aspects, clinical aspects to more practical aspects like medical visits reminders).

The clinician needs pointed are an agile system that allows a close follow up of the patients and a promptly identification of heart failure decompensations.

Additionally, big data and AI will be applied in all the process to:

- detect new risk parameters related to hospitalizations and mortality and quality of life deterioration
- allow for an individual and personalized risk assessment
- help decision support in these vulnerable and complex populations

Based on previous literature, patients, clinicians, and caregivers needs in the following paragraphs, a summary of the main variables that will be monitored is offered

4.1 Clinical study characteristics

After the designing the RETENTION platform, it will be validated through a Randomised Clinical Trial (RCT). The aim of this clinical study will be to investigate the effect of introducing continuous patient monitoring protocols outside hospitals and interventions informed by the analysis of the data collected through this monitoring on the following primary and secondary endpoints.

The primary endpoint will be death, heart failure hospitalisation or emergency room visit and patient quality of life. Secondary endpoints:

(a) All-cause mortality during the individual follow-up time (to a maximum of 575 days, i.e., the 547 days of the patient monitoring period plus 28 days from the final study visit)

(b) Cardiovascular mortality during the individual follow-up time (to a maximum of 575 days, i.e., the 547 days of the patient monitoring period plus 28 days from the final study visit)

(c) Days (%) lost due to unplanned cardiovascular hospitalisations during the individual follow-up time.

(d) Days (%) lost due to HF hospitalisations during the individual follow-up time.

(e) Change in the Minnesota Living with Heart Failure Questionnaire (MLHFQ) Global score between baseline (i.e., when a patient enters the study) and end of study.

(f) Change in the levels of N-terminal pro-B-type natriuretic peptide (NT-proBNP) between baseline and end of study.

(g) Change in the Depression score Patient Health Questionnaire 9 (PHQ-9) score between baseline and end of study.

(h) Change in the Carers Burden Questionnaire for Heart Failure (CBQ-HF) score between baseline and end of study

(i) Change in the Frailty Index For Elderly (FIFE [48] score between baseline and end of study)

In the study we will recruit a total of 450 patients across the six hospitals that will participate in the project. These patients will include: 200 patients with HF not enlisted for transplant at the time of their recruitment (i.e., approximately 44% of the total number of patients); 150 patients with LVAD (i.e., approximately 34% of the total number of patients); 100 heart transplant recipients (i.e., approximately 22% of the total number of patients).

Of these patients 225 patients will be the test group, referred to as remote patient monitoring and interventions group (RPMI group), and 225 patients will be the control group, referred to as remote patient monitoring and usual care (RPMUC group). The control and the test group for each site will have equal numbers of recruits in each of the above three categories of patients. Of the recruited patients, at least 30-35% will be women. This is because up until now, women have been underrepresented in most heart failure clinical trials, even though the disease prevalence remains generally the same between both sexes.

The inclusion criteria that will be used in the RCT will be:

- Overall:
  - Age: 18-75 years
  - able to understand and to consent to participating in the research; a score of > 22 on the Montreal Cognitive Assessment (MoCA; http://www.mocatest.org/), without cognitive impairment
  - with a depression score based on Personal health Qquestionnaire-9 (PHQ-9) score < 10
  - a frailty test score< 4
  - Written informed consent obtained.

- HF patients:
  - New York Heart Association (NYHA) class II or III
  - Left ventricular ejection fraction (LVEF) ≤ 40 %
  - At discharge after a HF hospitalization and up to 12 months after discharge
  - Not enlisted for heart transplant at randomisation
  - NTproBNP during the previous year ≥ 1000pg/mL

- VAD patients: Left Ventricular Assisted Device (LVAD) implantation as either destination therapy, bridge-to-transplant, or bridge to decision.

- Heart transplant recipients: Discharge following heart transplantation performed at least 30 days before randomization and not longer than 36 months.

Also, the following exclusion criteria will be applied:

- Acute coronary syndrome within the last 7 days before randomisation

- Planned cardiac surgery or percutaneous revascularisation, transcatheter aortic valve implantation, MitraClip and/or cardiac resynchronization therapy (CRT) implantation within 3 months after randomisation
- Revascularisation and/or CRT implantation within 28 days before randomisation
- Known alcohol or drug abuse
- Terminal renal insufficiency with haemodialysis
- Impairment or unwillingness to use the telemonitoring equipment
- Existence of any disease (other than cardiac disease) reducing life expectancy to less than 1 year
- Pregnancy
- Participation in other treatment studies or remote patient management programmes
- Patients on ambulatory inotropes (other than levosimendan) or intravenous medication

The RCT will be conducted based on the use of non-medical equipment including wearable devices and a smart phone that will be provided to the participants of both the test and the control groups by the project.

More details about the randomized clinical trial will be provided in the deliverable 8.2.

4.2 Variables to be monitored

The RETENTION platform should collect information from patients (HF, LVAD and HTx) and carers. The system will present this information to the patients to empower them in their disease management and to the clinical team. There will be an important space for interaction between the different actors.

In the following section, a detailed list of variables that based on clinical practice and state-of-art research should/could be monitored, the frequency when they will be monitored. High priority variables come mostly from clinical practice and are mandatory for a RETENTION. Intermediate ones are mostly variables for which according to the literature there is some significant evidence that can be associated with patient status; in this sense these are also to be included in RETENTION as they are expected to enhance the analysis of patient status. Finally, low priority variables are the ones that there is some evidence that can be associated to patient status; in this sense they are considered rather optional for RETENTION (at least during the project life cycle).

Table 3. Type of variables and devices used in RETENTION

Type of variable	Detailed variables	Device	Type of patient	Schedule	Priority	References
Vital signs	Blood pressure heart rate oxygen saturation Calculated variables: changes in vital signs, pulse pressure	Blood pressure cuff Saturometer	Heart failure Heart transplant (LVAD if possible)	Daily	High	(10–12,155)

Activity track	Steps, meters walked, other type of activities, continuous HR monitoring at baseline and during activity, time to recover	Smartwatch	Heart failure Heart transplant LVAD	Continuous	Intermediate	(26,78)
Sleep	Hours of sleep, sleep patterns and quality	Smartwatch	Heart failure Heart transplant LVAD	Daily	Intermediate	(181,182)
Symptoms	Fatigue, dyspnoea, oedema, orthopnoea, appetite, dizziness	Short and long questionnaires adapted for each type of patient	Heart failure Heart transplant LVAD	Short questionnaires daily Long questionnaires when change in symptoms	High	(10–12)
Medication compliance	Compliance	Alarms/reminders	Heart failure Heart transplant LVAD	According to medication schedule (BID, QD…)	High	(183–185)
Nutrition	Body weight, body composition Nutrition score	Weight scale MNA score	Heart failure Heart transplant LVAD	Daily	High	(186–188)
Depression	Depression symptoms	PHQ9	Heart failure Heart transplant LVAD Carer	Monthly	Intermediate	(189,190)
Cognitive status	Cognitive decline	MOCA	Heart failure Heart transplant LVAD	Monthly	Intermediate	(191,192)

Environmental variables	Temperature Humidity Pollution	Home sensors Local statistics	Heart failure Heart transplant LVAD	Continuous	Intermediate	(14–17)
Other environmental variables: Noise Sunlight exposure	Noise Sunlight exposure	Home sensors Questionnaires	Heart failure Heart transplant LVAD	Continuous	Low	(193)
Ventricular assist device related variables	VAD parameters: (flow, power, PI) Driveline exit care	Questionnaire Pictures	LVAD	Daily	High	(110,194)

5 Use cases and Scenarios

The presented use cases are associated with different end-user roles to be supported by the RETENTION solution (Global Insights Cloud – GIC, Clinical Site Backend - CSB, RETENTION Patient Edge or RETENTION Mobile application - App). Multiple roles can be associated with a same requirement. We identified the following roles:

- System Administrator or IT/administrative staff: it refers to the role that is responsible for the setup and reliable operation of the RETENTION Platform (GIC, CSB and App). It should be able to ensure that the uptime, performance, resources, and security of the computers they manage meet the needs of the other users. The system administrator may require access to the system components and to the registers accounting for the behaviour of the RETENTION Platform.
- Clinician or clinical expert: it refers to a health care professional that works as a primary clinical case manager of a patient. A clinician diagnoses and treats patients. The clinician uses the RETENTION platform in order to increase the level of evidence-based practices and care plans and has access to all patients associated to his/her Organisation.
- Patient: it refers to the patient gave consent to participate to the RETENTION study (RETENTION study participant). He/she interacts via the RETENTION Mobile application in order to acquire guidance or information about the treatment and the trajectory of personalised care plans.
- Carer or Caregiver: it refers to health professional (family caregiver, a respite caregiver, a home caregiver, or a primary caregiver) who provides care for the patient who needs extra help.
- Data Scientist: it refers to a professional responsible for collecting, analysing and interpreting the overall amount of data collected by the GIC.
- Healthcare policy maker: it refers to someone who exploits the statistical report and analytics resulting from the GIC to create policies and plans, especially for the good of a territory or community.
- Auditor: it refers to the role that is responsible for administering audits to the RETENTION platform (with the help of the admin, the DPO, and other project officials).

Summary of different use cases

Table 4. Summary of different use cases

Category	*Use case code*	*Name*
Clinician's use cases	RTCL01	**Creation of patient and data visualization**
	RTCL02	**Patient-doctor interactions**
	RTCL03	**Alarms**
	RTCL04	**Event record**
Patient's use cases	RTP01	**Daily data entry**
	RTP02	**Special variables**
	RTP03	**Special events**
	RTP04	**Automatic messages**
Carer's use cases	RTCA01	**Daily data entry**
	RTCA02	**Automatic messages**
Risk assessment generated by AI	RTBD01	**Risk assessment generated by AI**
Technical staff use cases	RTS01	**Dashboard End-user moderated registration**
	RTS02	**Dashboard End-user login**
	RTS03	**Manage end-user account information**
	RTS04	**Associating a device ID to a patient**
	RTS05	**Configuring a device and App**
	RTS06	**Managing Public health policy decision-making models**
	RTS07	**Performing GDPR compliance check**

5.1. Clinicians use case scenarios

5.1.1 Patient creation and data visualization

Table 5. Patient creation and data visualization

Use case code	**RTCL01**
Relation with other use cases	Predecessors: RTP01, 02, 03, 04, RTCA 01, 02, 03 Successors: RTCL 02, RTCL 03.
Name	**Creation of patient and data visualization**
Importance (priority)	Mandatory
Short Description	Clinical team check patients' data and alarms.
Objective	Purpose of this use case is to simulate data consultation for the clinicians
Actors	Clinicians

Dr. Elena Gómez is Mr. Rodriguez cardiologist. Dr. Gómez is a registered RETENTION user. She asked Mr. Rodriguez to participate in the RETENTION study during his last admission because she thinks it is the best way to improve her patient's quality of life and keep him out of the hospital. Mr. Rodriguez signs the informed consent to participate in the study.

Dr. Elena Gómez creates a new patient in the system. She selects the type of patient (HF, LVAD, HT) and adds the baseline and the relevant questionnaires (Ex: MOCA, medication scheme, management rules, personalized lifestyle recommendations and threshold values if applicable…)

The technical staff is informed by a ticket mechanism and gives the RETENTION devices and associates those to this patient.

Every morning when she arrives to the hospital she enters in her computer and opens the RETENTION dashboard. She enters her username and password and has access to Mr. Rodriguez data along with other patients from her organization.

She can easily track Mr. Rodriguez data as activity, sleep, weight, medications, … with graphs showing the most recent trends.

5.1.2 Patient-doctor interactions

Table 6. Patient-clinician interactions

Use case code	**RTCL02**

Relation with other use cases	Predecessors: RTCL01, RTP01, 02, 03, 04, RTCA 01, 02, 03 Successors: RTCL 03.
Name	**Patient-clinician interactions**
Importance (priority)	Mandatory
Short Description	Clinical team check patient´s data during the patient´s visit to HF clinic.
Objective	Purpose of this use case is to enter and store the information during a patient visit
Actors	1.-Clinicians 2.-Patients

Interaction between the patient and the clinician can be in in-person visits, telephone visits or chat through the platform.

Information related to the visits (vital signs, symptoms…) can be stored in the platform by the clinical team in the section “clinical visit”.

At the end of every interaction the doctor should select the final action that was taken from a predefined list of actions.

In the RETENTION intervention group, the clinical team will receive suggestions based on predefined rules for example: If mean heart rate is more than 70 bpm consider up titrating betablockers or if mean systolic blood pressure is higher than 100mmHg consider up titrating ACEi/ARB/ARNI). The clinical team must confirm the validity of the suggestion, update the medication and a notification will be sent to the patient through the mobile application.

In a more advanced version of the platform complex AI algorithms taking into account not only one measure of blood pressure and heart rate in the clinic but other variables as vitals variation, or activity track would be developed to better up titrate medications in HF patients.

5.1.3 Alarms

Table 7. Alarms

Use case code	**RTCL03**
Relation with other use cases	Predecessors: RTCL01, RTP01, 02, 03, 04, RTCA 01, 02, 03 Successors: RTCL 04.

Name	**Alarms**
Importance (priority)	Mandatory
Short Description	Clinical team receives a platform advice about important patients´ alarms.
Objective	Purpose of this is to detect patients´ decompensations
Actors	1.-Clinicians 2.-Patients

According to predefined thresholds alarms will be generated. Those alarms will appear in the dashboard whenever a clinician enters the platform. Every alarm will be accompanied by predefined actions the doctor must select.

For example, if an alarm has been generated because the patient has abnormally high blood pressure and the clinician increases the dose of losartan, he will then choose the action “change medication dose”.

In a second version of the platform notifications would be generated according to AI algorithms predicting the risk of adverse outcomes that must always be validated by the clinical team.

5.1.4 Event record

Table 8. Event record

Use case code	**RTCL04**
Relation with other use cases	Predecessors: RTCL01, 02, 03 RTP01, 02, 03, 04, RTCA 01, 02, 03
Name	**Event record**
Importance (priority)	Mandatory
Short Description	Clinical team will record every event occurring to the patient in a specific section in the platform.
Objective	Purpose of this is to record patient´s events in order to have a precise patient´s evolution monitoring
Actors	Clinicians

The clinical team will record every event occurring to the patient in a specific section in the platform. They will register the date, the type of event among a predefined list and other details related to it. For example, in the case of a heart failure admission dates of admission and discharge.

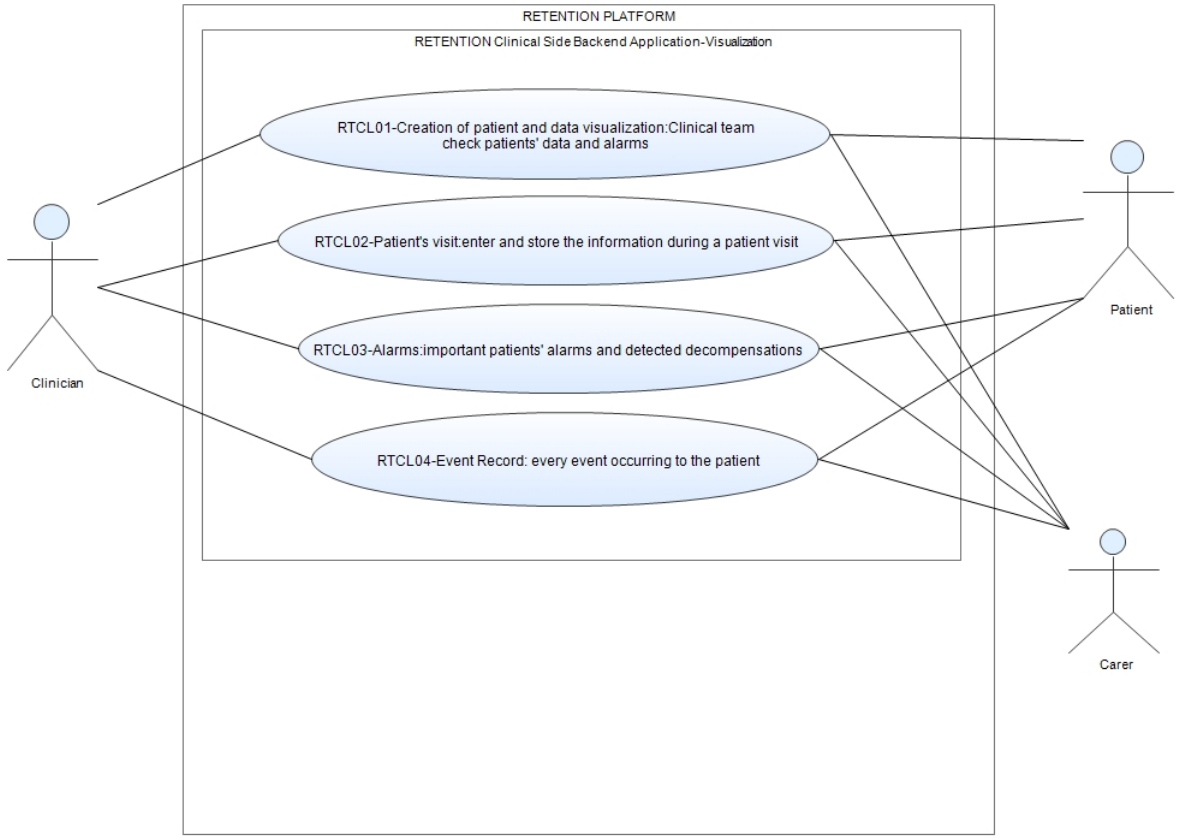

Figure 10. Clinician's use cases diagram

5.2. Patient's use cases

5.2.1 Daily data Entry

Table 9. Daily data Entry

Use case code	**RTP01**
Relation with other use cases	Predecessors: Successors: RTP 02, 03.
Name	**Daily data entry**
Importance (priority)	Mandatory
Short Description	Every day's entry of measurements and other data
Objective	Purpose of this use case is the patient's entry and storage of data in the platform

Actors	Patients

Assumptions

1. The patient owns credentials for the Retention platform.

Description

Mr. Rodriguez is a 70-year-old HF patient. He has been admitted recently for an acute decompensation. At discharge he meets all the inclusion criteria and none of the exclusion criteria for the RETENTION study. His clinician asks him to participate, and Mr. Rodriguez accepts signing the informed consent.

Prior to discharge, Mr. Rodriguez answers initial questionnaires about his quality of like (MLWHF, KCCQ), nutrition (MNA), depression (PHQ9), cognitive status (MOCA). The clinician responsible fills the baseline variables regarding prior HF history and comorbities, laboratory values, echocardiographic parameters, etc. He also enters in the platform the treatment the patient has to follow at discharge (medication, doses, and the time when he has to take them), to set the reminders/alarms (optimal/extreme ranges).

Mr. Rodriguez is provided with a tablet and other devices to monitor his vital signs (ex: a smartwatch, a saturometer…)

Every morning, when he wakes up at 8 am, he opens the RETENTION platform. He enters his username and password. He weights himself, measure his blood pressure and his oxygen saturation. These data, and data about the previous day activity (steps, meters walked…), hours and quality of sleep and data from home sensors and local statistics are transferred directly to the platform via Bluetooth and stored. The RETENTION platform asks him a short question: “how are you feeling today?”, he answers “same,  ”.

At 9 am he switches off the alarm and confirms he has taken his morning pills (carvedilol and sacubitril/valsartan). At 12 am and 9 pm he does the same confirming he has taken his midday and evening pills.

Most of the variables will be common to every of the 3 types of patients, however, LVAD patient will manually enter every day their LVAD parameters (Flow, Pump speed, PI, Power, alarms).

5.2.2 Special variables

Table 10. Special variables

Use case code	**RTP02**
Relation with other use cases	Predecessors: RTP 01 Successors: RTCL 03, RTCL04.

Name	**Special variables**
Importance (priority)	High
Short Description	Variables that are not daily monitored
Objective	Purpose of this use case is the patient's entry and storage of data in the platform
Actors	1.-Patients 2.-Clinicians

Some variables as questionnaires will be only replied once a month. A reminder will be sent to the patient to fill the questionnaires.

In the case of LVAD patients, every time driveline exit wound care is undertaken (very 3-5 days for example) a picture of the driveline exit will be sent through the platform to the clinical team.

5.2.3 Special events

Table 11. Special events

Use case code	**RTP03**
Relation with other use cases	Predecessors: RTP03 Successors: RTP 05. RTCL03
Name	**Special event**
Importance (priority)	Mandatory
Short Description	Advice to the clinicians of worsening of symptoms notifying it in the platform
Objective	Purpose of this use case is the patient's entry and storage of data in case of a special event
Actors	1.-Patients 2.- Clinical team

The patient is able, every time he experiences a change in his symptoms to enter his vital signs and symptoms under the "special events" section.

The RENTENTION platform will send an automatic message "The information is stored and will be sent to your clinical team, however, remind to contact the emergency services if symptoms persist or become worse".

Artificial intelligence will be used to find patterns between all the previously mentioned variables that can predict those special events, hospitalizations, or other outcomes.

5.2.4 Automatic messages

Table 12. Automatic messages

Use case code	**RTP04**
Relation with other use cases	Predecessors: RTP04. Successors: RTP 04,05.
Name	**Automatic message**
Importance (priority)	Mandatory
Short Description	Platform reminders to improve patient`s adherence to the program.
Objective	Purpose of this use case is to establish the triggers for automatic messages
Actors	1.-Patients

Example

Mr. Rodriguez is on holidays, and he has forgotten to entry data in RETENTION for the past two days. He receives an automatic message from the platform: “Mr. Rodriguez, we have not been receiving your information in the past two days, it is important to track your clinical parameters to maintain stability and for your medical team to be up to date”.

Mr. Rodriguez continue his holidays entering every day his clinical parameters. He receives then an automatic message “Congratulations, you are very compliant with the RETENTION platform, a good self-management is important to maintain a good health status!”

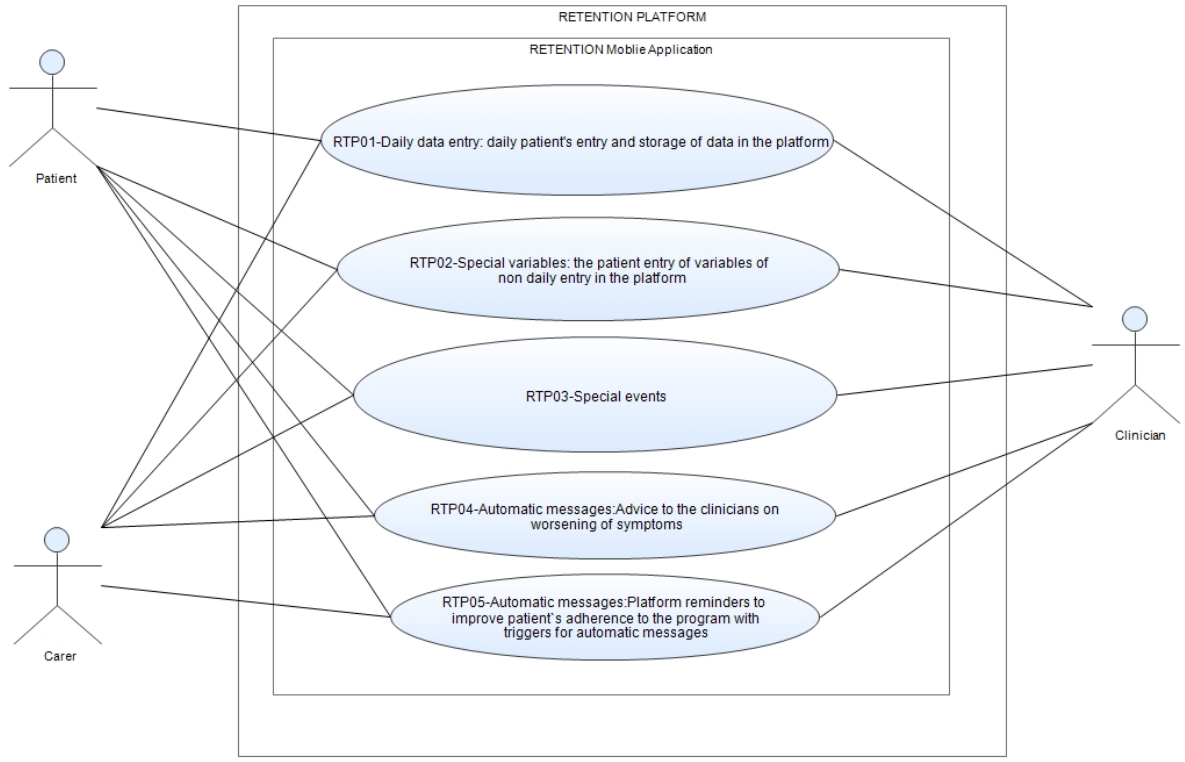

Figure 11. Patient's use cases diagram

5.3. Carer use case scenarios

5.3.1 Daily data entry

Table 13. Caregiver Daily data entry

Use case code	**RTCA01**
Relation with other use cases	Predecessors: Successors: RTCA02
Name	**Daily data entry or monthly reply to questionnaires**
Importance (priority)	Mandatory only for LVAD patients.
Short Description	The caregiver can complete patient's data and mus complete his/her own questionnaires
Objective	Purpose of this use case is to entry and store the information collected by the patient caregiver

Actors	1.-Caregivers

The caregiver will use the same device to track the patient's variables in case of patients that need assistance. Caregivers will have their own profile on the platform.

They will also have to provide some variables as questionnaires related to their own well-being.

The RENTENTION platform send an automatic message "The information is stored and will be sent to your clinical team, however, remind to contact the emergency services if symptoms persist or become worse".

5.3.2 Automatic messages

Table 14. Caregiver Automatic messages

Use case code	**RTCA02**
Relation with other use cases	Predecessors: RTP03. Successors:
Name	**Automatic message**
Importance (priority)	Mandatory
Short Description	Platform advice
Objective	Purpose of this use case is to establish the automatic messages the caregiver is going to receive
Actors	1.-Caregivers 2.-Clinicians

Maria is receiving all the automatic messages that Pedro receives from the platform: rewarding his adherence or activity increase or warning his non-adherence to the platform.

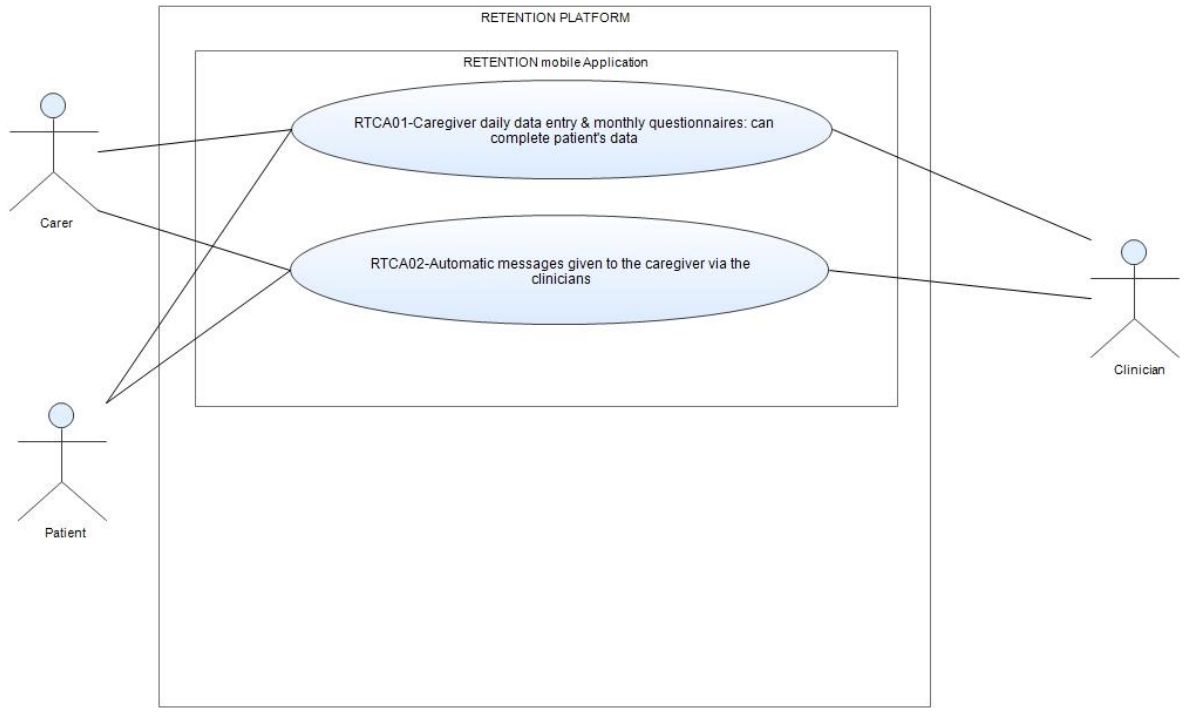

Figure 12. Carer's use cases Diagram

5.4. Risk assessment generated by AI

Table 15. Risk assessment generated by AI

Use case code	**RTBD01**
Name	**Risk assessment generated by AI**
Importance (priority)	Mandatory
Short Description	Thanks to RETENTION system new parameters related to HF/LVAD/transplantation outcomes will be identified.
Objective	Use the big data and AI in the RETENTION solution
Actors	1.-Clinicians 2.-Patients 3.-Caregivers

The RETENTION platform offers an innovative way of collecting data from traditional HF, HT, and LVAD related variables and new potential predictors such as temperature, pollution that are continuously monitored. AI will be used to describe patterns and identify new risk profiles.

All these parameters will be integrated to offer a continuous and personalized risk assessment and support for:

- Predicting
    - HF decompensations
    - overall mortality
    - LVAD complications as driveline infections, bleeding, or pump thrombosis
    - HT rejection or infections
- Ensuring INR correct levels
- Generating better medication titration protocols
- Reduce in-person visits while improving patient's care

Algorithms will be continuously refining as more data is entered in the platform, and clinicians would be constantly updated.

A decision support system would be put in place with personalized advice that would be validated by the clinicians.

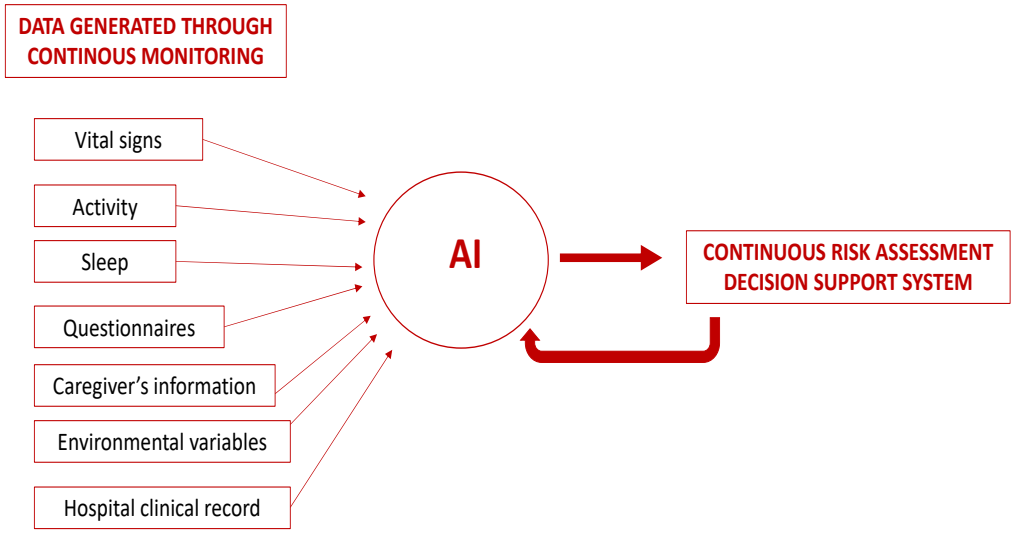

Figure 13. Risk assessment generated by AI

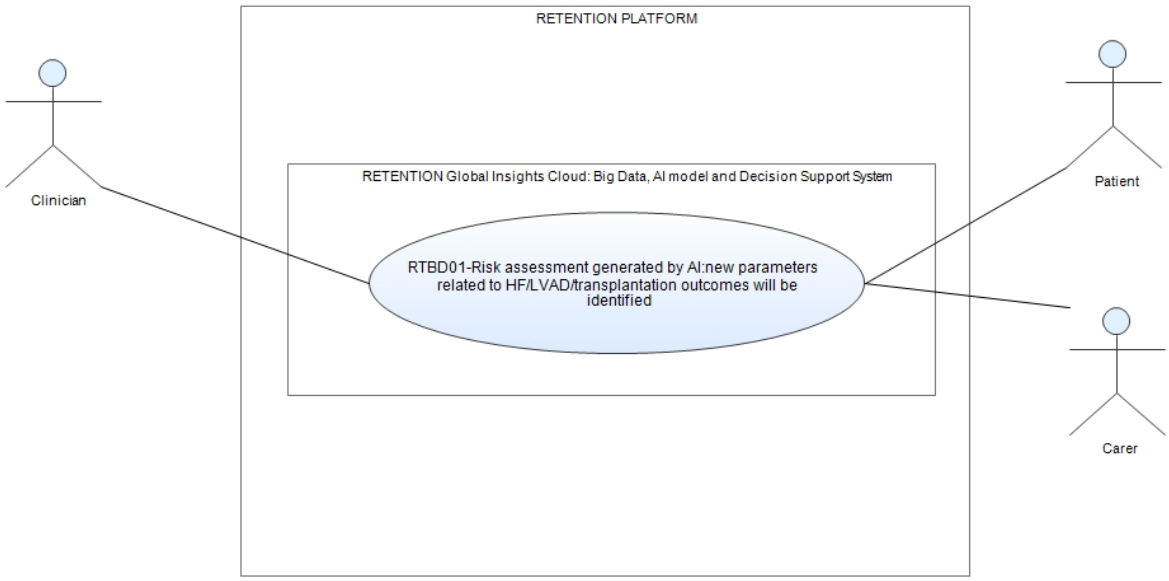

Figure 14: Risk assessment diagram

5.5. Technical use cases

5.5.1 Dashboard End-user moderated registration

Table 16. Dashboard End-user moderated registration

Use case code	**RTS01**
Relation with other use cases	Predecessors: Successors: RTS02
Name	**Dashboard End-user moderated registration**
Importance (priority)	Mandatory
Short Description	Moderated by administrator registration of an end-user
Objective	An end-user registers to gain access to the RETENTION Dashboard
Actors	System Administrators All retention valid end-users

Assumptions

1. The end-user has a valid email account

2. The system administrator has a list from each participating organisation of all valid end-users (full name, Pilot, Organisation, role, valid email) allowed to utilise the RETENTION Platform

Description

Ms. Papadopoulou is a clinician in Onassis Cardiac Surgery Center and participates in the RETENTION study (Greek Pilot). She is among those responsible to administer records of Greek pilot patients, and her name is included in the list previously handed to the RETENTION Platform administrator.

Ms. Papadopoulou visits the registration page and fills all required fields (desired username, email, first name, last name, Organisation, Pilot, preferred role, and password). System checks if the username is not already in use and prompts accordingly. Then she checks the reCAPTCHA checkbox (to indicate than a human performs this registration task) and confirms that she read and understood the Privacy Policy (a link to this or a textarea including this text is provided). If the information she entered is valid, and the username she picked has not been used by another RETENTION end-user, the RETENTION Platform will register the new end-user with the given parameters. Upon successful initial registration, she will receive an email (produced by RETENTION platform automatically) to verify that she is the owner of the email used. At this point, this end-user account has status "Unverified".

Upon confirmation of the validity of the email (status "Verified") by her, the Administrator can view this newly created registration record, check against the information presented in the list for the specific Organisation (e.g., correcting the end-user role), and proceed in its activation (change status to "Active"). Doing so, Ms. Papadopoulou will receive an email notifying that her RETENTION Platform account has been activated and she may use e-services offered. Then she (as any valid RETENTION end-user) may login by entering the username and password she chose.

At any time and for various RETENTION administration reasons, the Administrator may temporarily deactivate a RETENTION end-user account (status "Inactive"), suspended it (status "Suspended"), or indicate that this account has been permanently expired (status "Expired"). In any case of change of status, the end-user is notified by email.

5.5.2 Dashboard End-user login

Table 17. Dashboard End-user login

Use case code	**RTS02**
Relation with other use cases	Predecessors: RTSA01 Successors: All services limited to the scope of each end-user role and Organisation
Name	**Dashboard End-user login**
Importance (priority)	Mandatory

Short Description	A valid end-user signs in the system
Objective	A valid RETENTION Platform end-user signs in the system to use available (to his/her role and Organisation scope) services
Actors	System Administrators Dashboard end-users (all roles supported)

Assumptions

1. Valid RETENTION Platform end-user account

Description

Ms. Papadopoulou is a clinician in Onassis Cardiac Surgery Center and valid RETRENTION Platform end-user. She accesses the sign-in function of the RETENTION Platform, and the system prompts for her login credentials (username and password). Upon typing those, she checks also the reCAPTCHA checkbox (to indicate than a human performs this registration task).

The system validates the entered credentials making sure that they match with the respective user account in the system. If so, the system displays the signed-in end-user Home Page.

If an end-user forgets his/her username or password, he/she may trigger the Recover Username or Password service. Doing so, the system will prompt the end-user to type again his/her personal info, the email provided when the account was created, and the Organisation is associated with. Provided that those are answered correctly, the username or a link for changing the password will be emailed to the specific email address.

5.5.3 Manage end-user account

Table 18. Manage end-user account

Use case code	**RTS03**
Relation with other use cases	Predecessors: RTS01, RTS02. Successors: All services limited to the scope of each end-user role and Organisation
Name	**Manage end-user account information**
Importance (priority)	Mandatory
Short Description	End-user manages his/her personal information and login credentials

Objective	Allows all valid RETENTION Platform end-users to update user account information maintained in their user's account records
Actors	Dashboard valid end-users (all roles supported)

Assumptions

1. Valid RETENTION Platform end-user account

Description

Ms. Papadopoulou is a clinician in Onassis Cardiac Surgery Center and valid RETRENTION Platform end-user. For whatever reason, she wants to reset her password. She triggers the system function (e.g., Profile link) that enables her to update the information that is maintained in the User's account.

The system displays the end-user account information currently stored for her. Ms. Papadopoulou selects the 'Reset/Change password' option, enters a new password and confirmation of new password, and then requests that the system saves it.

System validates if current password, new password, and new password confirmation are the same. Afterwards, the system validates if new password meets the complexity rules been defined. If rules are met, and new password and new password confirmation are the same, the hashed password is stored, and then the system sends an email notification about this change.

5.5.4 Associating a device ID to a patient

Table 19. Associating a device ID to a patient

Use case code	**RTS04**
Relation with other use cases	Predecessors: RTS01, RTS02, RTS03 Successors: RTS05
Name	**Associating a device ID to a patient**
Importance (priority)	Mandatory
Short Description	Pairing a smartphone and other devices/sensors with a patient via a device ID and patient's RETENTION identification Managing the status of the previously paired smartphone and other devices/sensors
Objective	To allow a successfully paired and active smartphone to

	transmit patient's usage data and receive personalised data, notifications and interventions produced by the RETENTION Platform
Actors	Clinicians

Assumptions

1. Patient met recruitment criteria

Description

During the recruitment (or after a short period of time), Dr. Gomez (clinician who recruited Mr. Rodriguez) logins to the RETENTION platform and enters smartphone ID (unique IMEI) and smartwatch ID (unique IMEI or GUID or other device identifier) to Mr. Rodriguez personal record via the Device Management. Paired devices will be handed to him as soon as configuration process (initialisation, App installation, administrative work, etc.) is completed.

At any time and for various administration reasons (e.g., device malfunction, lost or stolen device), Dr. Gomez may temporarily or permanently deactivate the device, and/or proceed in creating a pairing record for a new one.

5.5.5 Configuring a device and App

Table 20. Configuring a device and App

Use case code	**RTS05**
Relation with other use cases	Predecessors: RTS01,02,03,04. Successors:
Name	**Configuring a device and App**
Importance (priority)	Mandatory
Short Description	Managing the status of the previously paired smartphone and other devices/sensors Installing/configuring the App
Objective	To allow a successfully paired and active smartphone to transmit patient's usage data and receive personalised data, notifications and interventions produced by the RETENTION Platform
Actors	System Administrators

Assumptions

1. Paired devices have been identified

Description

During the recruitment (or after a short period of time), Ms. Alonso (technical staff, Dr. Gomez's colleague) logins to the RETENTION platform and views associated devices to patient Pseudo-Id1 (unique ID associated to Mr. Rodriguez record) without usage metadata been indicated. Ms Alonso does not have access to the patient's name, Personal Identifiers Information, or any information stored in his personal health record.

The System displays the Pseudo-Id1, types of devices and their status of all patients (within the scope of Ms. Alonso Organisation) currently stored in the System. Ms. Alonso views newly created or updated records of paired devices/sensors for the Pseudo-Id1 associated to Mr. Rodriguez and selects the device wants to configure.

She checks and confirms the unique ID of the smartphone (IMEI) stored in the system and then enters this Pseudo-Id1 and the randomly assigned email (to be used for automatically triggering the Update mechanism of the App) in the configuration settings of the specific smartphone to be handed Mr. Rodriguez (during the installation, or later on). She also assigns value for each parameter that can be configured in the App.

She proceeds with the configuration process for all associated devices to the specific smartphone.

Upon successful completion, she defines the status for all of them as active (thus, allowing the smartphone to transmit usage data to and receive data from the CSB).

5.5.6 Managing Public health policy decision-making models

Table 21. Managing Public health policy decision-making models

Use case code	**RTS06**
Relation with other use cases	Predecessors: Successors:
Name	**Managing Public health policy decision-making models**
Importance (priority)	Mandatory
Short Description	Managing public health policy decision-making models and the execution of data analytics tasks which constitute them
Objective	To allow the formation and execution of analytics in order to validate Policies associated to previously executed Data Analytics Workflows

Actors	Data Scientists Healthcare policy makers

Assumptions

1. Pseudonymised data transferred from CSBs to GIC

Description

Mr. Karl Rummenigge (data analyst) pre-processed (removed outliers, filter) and analysed via the GIC Dashboard a dataset containing the medical records and usage data (daily min and max blood pressure, daily average heart rate, daily average oxygen saturation, daily average body temperature, daily average, pulse pressure, daily average steps, daily nutrition, daily cognitive decline, temperature, humidity and particulate matter air pollution levels PM2.5) for patients living in the residential area of Essen and Athens.

He performed Statistical quantitative description of the category and numeric features. Then he applied Random Forests. As input for the training, he randomly chose 70% of the dataset and used the remaining 30% for the test set. He also employed Linear Regression and compared the prediction results. Estimates showed a small significant decrease in diastolic and systolic blood pressure in association with particulate air pollution. In parallel, heart transplant recipients who had long-term exposure to air pollution (Athens) had a higher risk for mortality due to infection for every 10 mg/m3 increase in PM2.5 levels in comparison to those not been exposed (Essen).

5.5.7 Performing GDPR compliance audit

Table 22. Performing GDPR compliance audit

Use case code	**RTS07**
Relation with other use cases	Predecessors: RTS01,02,03,04,05 Successors:
Name	**Performing GDPR compliance check**
Importance (priority)	Mandatory
Short Description	Reviewing GDPR rights status and supplementary evidence
Objective	GDPR Compliance
Actors	Patients System Administrators Auditors

Assumptions

1. Patient has exercised his/her Right of access

Description

Upon receipt of a “Right of access"-type request by Mr. Rodriguez (patient), Mr. Vasilis Xatzipanagis (System Administrator) has started to compile the information as for who and when RETENTION end-users performed actions (view/edit/delete) to his personal data:

- IDs, PIIs stored in an encrypted repository
- Personal health record and usage data stored in FHIR repository

Upon completion of the task, Mr. Vasilis Xatzipanagis he provided (via the App) the information requested in an accessible, user-friendly format.

During this period, Dr. Cardano (Auditor) was able to track the progress (status) of the request, view who has been working on it and request (if he wanted) logs that confirmed the complied list (aggregations).

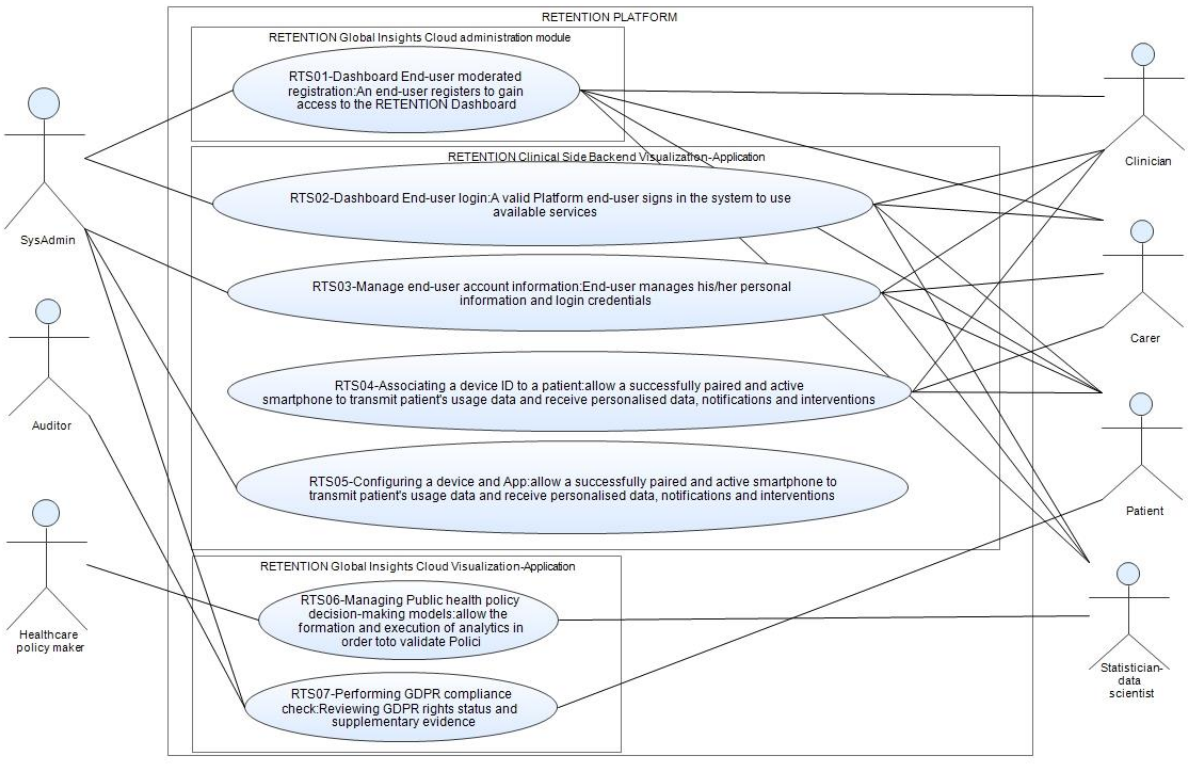

Figure 15. Technical staff use cases diagram.

6 Functional & non-functional requirements analysis

A further aspect to be highlighted is that the documentation developed by the activities carried out has focused on elicitation functional requirements, but non-functional requirements also emerged during the focus groups and the evaluation meetings involving clinical and technical partners. A first group of non-functional requirements is related to security and legal aspects.

The output obtained by the Focus Groups with patients and clinicians has underlined that usability, acceptance and integration aspects must be addressed by the project with specific care. Making the system capable to adapt to different user's viewpoints is critical of the project.

One of the most crucial parts of a new system, is to meet the expectations of the users. The RETENTION system will have to meet and exceed the expectations of the users for its critical success. The part of requirement analysis is the second part of the foundation of a great user- centered system.

The RETENTION system, will strive to use a complete User-Centred design (UCD), by solving the problem in question by focusing and understanding the people and their needs.

Among the key objectives of the RETENTION Work Package 3 is to collect and analyse requirements from the users being part of the RETENTION ecosystem. The requirements are defined as:

- Functional requirements (FN), which are associated with the capability or application needed to directly
  support the users' accomplishment of their mission and tasks, and
- Non-Functional requirements: (NF), which are mainly general requirements, typically implicit and technical in nature and emerge as system requirements to satisfy the users' functional needs, e.g., availability, quality of service, timeliness, and accuracy.

In the next sections, the non-functional (technical requirements) and the functional requirements of the RETENTION system are provided.

Non-Functional Requirements

6.1 Usability requirements

A system can have adequate functionality, but inadequate usability because it is too difficult to use. The usability requirements specify how easy the system must be to use.

Requirement ID:	**NF_US_01**	Priority:	Mandatory
Requirement title:		Ease of learning	
Description:		The functionalities and interfaces offered by the RETENTION platform should be easy to learn by all types of users. New users should be able to learn all the functionalities offered with minimum supervision.	
Rationale/Goal:		To ensure the quick adoption of new platform's users, without need for extensive trainings.	
Means of verification:		Usability Testing	
Dependencies:		NF_US_05	

Requirement ID:	**NF_US_02**	Priority:	Mandatory
Requirement title:		Responsive Interface	
Description:		User friendliness and responsiveness of the interface will be accomplished.	
Rationale/Goal:		User friendly, use in different machines (display)	
Means of verification:		Screen available in pc screen and phone/tablet display. Unit testing.	
Dependencies:		NF_US_03, NF_US_04	

Requirement ID:	**NF_US_03**	Priority:	Mandatory
Requirement title:		Personalized interface	
Description:		The interface will be able to morph into the user requirements.	
Rationale/Goal:		Personalized treatment and information.	
Means of verification:		Dynamic way of defining the interface items. Unit testing.	
Dependencies:		NF_US_02	

Requirement ID:	**NF_US_04**	Priority:	Mandatory
Requirement title:		Usability by design	
Description:		RETENTION and its components should be designed to meet high usability.	
Rationale/Goal:		High usability.	
Means of verification:		User Satisfaction.	
Dependencies:		NF_US_02, NF_US_03	

Requirement ID:	**NF_US_05**	Priority:	Mandatory
Requirement title:		User guidance.	
Description:		RETENTION shall guide the user to the correct choices (wizards, list of possible values, non-modal windows, etc.).	
Rationale/Goal:		Task efficiency.	
Means of verification:		Task performance. Unit test.	
Dependencies:		NF_US_01	

Requirement ID:	**NF_US_06**	**Priority:**	**Optional**
Requirement title:		System Ergonomics: Multiple end-users devices support	
Description:		The UI of any part of the RETENTION system should adapt to the screen resolution that the users are executing.	
Rationale/Goal:		Ability to view and execute tasks on the RETENTION system, in different devices and screen resolution requirements on the available device.	
Means of verification:		Usability test with multiple devices. Unit testing.	
Dependencies:		NF_US_02, NF_US_03	

Requirement ID:	**NF_US_07**	Priority:	Mandatory
Requirement title:		Visualization of the user's data.	
Description:		RETENTION shall use visualization techniques for users' data, to be easier to read by the user.	
Rationale/Goal:		User satisfaction.	
Means of verification:		User Satisfaction.	
Dependencies:		NF_US_01, NF_US_02, NF_US_03, NF_US_04	

Requirement ID:	**NF_US_08**	Priority:	Optional
Requirement title:		W3C compliant	
Description:		User friendliness of the interface for disability will be accomplished.	
Rationale/Goal:		User friendly for users with disabilities.	
Means of verification:		W3C certification process.	
Dependencies:		NF_US_01, NF_US_02, NF_US_03, NF_US_04	

6.2 Performance requirements

Requirement ID:	**NF_PR_01**	**Priority:**	**Mandatory**
Requirement title:		System time response	
Description:		The time response of the RETENTION system and its components should not degrade with an increase in available datasets and models execution.	

Rationale/Goal:	Ensure system performance and stability under all conditions of the system and full data availability to the users.
Means of verification:	Performance testing. System test.
Dependencies:	NF_PR_02

Requirement ID:	**NF_PR_02**	**Priority:**	**Mandatory**
Requirement title:		Performance: System Capacity	
Description:		The capacity should be more than adequate for the system, without degradation in performance of the RETENTION system and its components. It should not degrade with an increase in new and available datasets.	
Rationale/Goal:		Ensure system capacity under all conditions of the system and full data availability to the users.	
Means of verification:		Performance testing. System test.	
Dependencies:		NF_PR_01	

Requirement ID:	**NF_PR_03**	**Priority:**	**Mandatory**
Requirement title:		Performance: Concurrent users	
Description:		The system must support multiple users at the same time.	
Rationale/Goal:		Ensure responsiveness and stability under a full workload	
Means of verification:		Performance testing for server request processing times and acceptable concurrent user volumes. Acceptance tests – stress test.	
Dependencies:		NF_PR_01, NF_PR_02	

Requirement ID:	**NF_PR_04**	**Priority:**	Mandatory
Requirement title:		Operational: smooth and seamless RETENTION system components interactions	
Description:		The RETENTION system should expose integration layers, capable for exchanging data and models between its components (e.g., through API interfaces, stream-processing bus etc).	
Rationale/Goal:		Smooth and Seamless data flow between the RETENTION system components	
Means of verification:		By design and Performance and usability testing	
Dependencies:		NF_PR_01, NF_PR_02, NF_PR_03, NF_PR_04	

Requirement ID:	**NF_PR_05**	**Priority:**	Mandatory
Requirement title:		Performance: Loading time	
Description:		The system needs to perform each function of the end user in under **15** seconds	

Rationale/Goal:	Ensure user experience
Means of verification:	Calculation of the time taken to completely display the content of a specific page. User tests. units testing.
Dependencies:	NF_PR_01

Requirement ID:	**NF_PR_06**	Priority:	Mandatory
Requirement title:		Performance: System Uptime	
Description:		The system needs to have at least a 99.5% uptime and should be available, up and running 24x7, no matter the time zone.	
Rationale/Goal:		Ensure system reliability	
Means of verification:		By design. Server report. Stress tests.	
Dependencies:		NF_PR_01, NF_PR_02, NF_PR_03, NF_PR_05	

Requirement ID:	**NF_PR_07**	Priority:	Mandatory
Requirement title:		Dashboard performance	
Description:		Speed and data accuracy for data entry.	
Rationale/Goal:		Not annoying to users	
Means of verification:		Meet the specs of the project. modules tests. System test. Applications tests.	
Dependencies:		NF_PR_01, NF_PR_02, NF_PR_03, NF_PR_04, NF_PR_05	

Requirement ID:	**NF_PR_08**	Priority:	Mandatory
Requirement title:		AI model performance	
Description:		Speed of the AI model, when running on dataset.	
Rationale/Goal:		To give fast and accurate responses to the doctor/decision maker	
Means of verification:		Meet the specs of the project. by design. Unit testing. System testing.	
Dependencies:		NF_PR_01, NF_PR_03, NF_PR_05, NF_PR_07	

6.3 Availability and reliability requirements

Requirement ID:	**NF_AR_01**	Priority:	Mandatory
Requirement title:		Dashboard (top level)	
Description:		Availability of the system to take information at any time and give information at any time.	
Rationale/Goal:		To be always available for getting and processing data with 99.5% availability	
Means of verification:		Availability by design. System testing. Unit testing.	
Dependencies:		NF_PR_06	

Requirement ID:	**NF_AR_02**	Priority:	Mandatory
Requirement title:		back end	
Description:		Availability of the system to take information at any time and give information at any time.	
Rationale/Goal:		To be always available for getting and processing data with 99.5% availability	
Means of verification:		Availability by design. System testing. Unit testing.	
Dependencies:		NF_PR_06, NF_AR_01	

Requirement ID:	**NF_AR_03**	Priority:	Mandatory
Requirement title:		Edge gateway	
Description:		Availability of the edge computing software and system with 99.5% availability on the server side. The results that are provided to the users by the Edge gateway component should be accurate and reliable (sensitivity, specificity, precision etc.).	
Rationale/Goal:		To be always available for recording measures	
Means of verification:		Availability by design. System testing. Unit testing.	
Dependencies:		NF_PR_06, NF_AR_01, NF_AR_02	

Requirement ID:	**NF_AR_04**	Priority:	Mandatory
Requirement title:		Web application	
Description:		Availability of the web application software and system with 99.5% availability	
Rationale/Goal:		To be always available for recording measures	
Means of verification:		Availability by design. System testing. Unit testing.	
Dependencies:		NF_AR_01, NF_AR_02, NF_AR_03	

Requirement ID:	**NF_AR_05**	Priority:	Mandatory
Requirement title:		Phone/tablet application	
Description:		Availability of Phone/tablet software and system	
Rationale/Goal:		To be always available for recording measures	
Means of verification:		Availability by design. System testing. Unit testing.	
Dependencies:		NF_AR_04	

6.4 Legal and Ethical requirements

Requirement ID:	**NF_LE_01**	**Priority:**	**Optional**
Requirement title:		Privacy of cloud data	
Description:		Data stored in the Backend platform are pseudonymized (IDs, end-user registration information) and anonymised (usage data, medical records, analytics, interventions)	
Rationale/Goal:		Data privacy	
Means of verification:		legal requirements tests, by design and continuous monitoring	
Dependencies:		NF_LE_02, NF_LE_05	

Requirement ID:	**NF_LE_02**	Priority:	Mandatory
Requirement title:		Consent for Personal Data	
Description:		Even though a consent will be signed before to start using the system, the consent will be also acknowledged and “signed” (check boxed date and name) on the first time the application is executed.	
Rationale/Goal:		Data privacy.	
Means of verification:		legal requirements tests, unti tests, by design and continuous monitoring	
Dependencies:		NF_LE_01, NF_LE_05	

Requirement ID:	**NF_LE_03**		Mandatory
Requirement title:		Implement “Privacy by Design”	
Description:		The RETENTION Project (i.e., platform, app, management procedures been supported by digital means) shall implement appropriate technical and organisational measures which are designed to implement the data protection principles (lawfulness, fairness & transparency; purpose limitation; data minimization; accuracy; storage limitation; integrity & confidentiality; accountability).	
Rationale/Goal:		Data privacy.	
Means of verification:		By design and continuous monitoring. legal requirements test	
Dependencies:		NF_LE_01, NF_LE_02, NF_LE_04	

Requirement ID:	**NF_LE_04**		Mandatory
Requirement title:		Implement “Privacy by default”	

Description:	The RETENTION Project (i.e., platform, app, management procedures been supported by digital means) shall implement, per processing activity, appropriate technical and organizational measures which are designed to implement data-protection principles and that ensure that by default only personal data which are necessary for each specific purpose of the processing are processed.
Rationale/Goal:	Data privacy.
Means of verification:	By design and continuous monitoring. legal requirements test
Dependencies:	NF_LE_01, NF_LE_02, NF_LE_03

Requirement ID:	**NF_LE_05**	Priority:	Mandatory
Requirement title:		GDPR compliance	
Description:		The RETENTION Project (i.e., platform, app, management procedures been supported by digital means) shall implement appropriate measures to ensure and to be able to demonstrate compliance with the data protection and security legal framework.	
Rationale/Goal:		Data privacy	
Means of verification:		By design and continuous monitoring. legal requirements test	
Dependencies:		NF_LE_01, NF_LE_02	

Requirement ID:	**NF_LE_06**	Priority:	Mandatory
Requirement title:		Respect data subject rights	
Description:		The RETENTION Project (i.e., platform, app, management procedures been supported by digital means) shall, among others by means of appropriate technical and organisational measures, allow for data subjects to exercise their rights in relation to the processing of their personal data.	
Rationale/Goal:		Data privacy	
Means of verification:		By design and continuous monitoring. legal requirements test	
Dependencies:		NF_LE_05	

Requirement ID:	**NF_LE_07**	Priority:	Mandatory
Requirement title:		Maintain records of processing activities	
Description:		The RETENTION platform shall maintain records of processing activities.	

Rationale/Goal:	Data privacy
Means of verification:	By design and continuous monitoring. legal requirements test, unit test, system test, intergration tests
Dependencies:	NF_LE_04, NF_LE_05

Requirement ID:	**NF_LE_08**	Priority:	Mandatory
Requirement title:		Notify and communicate personal data breaches	
Description:		The RETENTION Project (i.e., platform, app, management procedures been supported by digital means) shall take all necessary measures to detect security and data incidents, and to allow for the notification of personal data breaches to the supervisory authority and, if necessary, to the data subjects.	
Rationale/Goal:		Data privacy	
Means of verification:		By design and continuous monitoring. legal requirements test	
Dependencies:		NF_LE_05, NF_LE_06	

Requirement ID:	**NF_LE_09**	Priority:	Mandatory
Requirement title:		Implement pseudonymisation, anonymization or deletion	
Description:		The RETENTION Platform shall pseudonymise, anonymize or delete personal data, where deemed appropriate, in order to comply with the core data protection principles	
Rationale/Goal:		Data privacy	
Means of verification:		By design and continuous monitoring. legal requirements test. Unit testing. System test.	
Dependencies:		NF_LE_05	

6.5 Security and Privacy requirements

Requirement ID:	**NF_SP_01**	Priority:	Mandatory
Requirement title:		Role-based access control (RBAC)	
Description:		Accessibility – Platform shall provide the data access according to security and privacy policies. Limit access to information and information processing facilities, using role based access control.	
Rationale/Goal:		Privacy and security.	

Means of verification:	Legal requirements testing. Units testing. Systems testing.
Dependencies:	NF_LE_03

Requirement ID:	**NF_SP_02**	Priority:	Mandatory
Requirement title:		Role-based access control (RBAC)	
)Description:		Platform shall provide mechanisms to configure security and privacy policies	
Rationale/Goal:		Privacy and security.	
Means of verification:		Legal requirements testing. Units testing. Systems testing.	
Dependencies:		NF_LE_03	

Requirement ID:	**NF_SP_03**	Priority:	Mandatory
Requirement title:		Data backup	
Description:		Platform will facilitate mechanism for storage facilities of all usage data and log files	
Rationale/Goal:		Privacy and security.	
Means of verification:		Units testing. Systems testing.	
Dependencies:		NF_LE_07	

Requirement ID:	**NF_SP_04**	Priority:	Mandatory
Requirement title:		Effectiveness	
Description:		Platform will support secure, private and trust exchanging of data among different entities (i.e., smartphones, services).	
Rationale/Goal:		Privacy and security.	
Means of verification:		By design. Units testing. Systems testing. Acceptance tests	
Dependencies:		NF_LE_06	

Requirement ID:	**NF_SP_05**	Priority:	Mandatory
Requirement title:		REST API	
Description:		Platform will implement REST API to facilitate the data exchange with entities (i.e., smartphones, services).	
Rationale/Goal:		Privacy and security.	
Means of verification:		By design. Units testing. Systems testing. Acceptance tests.	
Dependencies:		NF_SP-01	

Requirement ID:	**NF_SP_06**		Mandatory
Requirement title:		Communication channel security	

Description:	Platform must guarantee the secure communication with a total of 450 end-users simultaneously.
Rationale/Goal:	Privacy and security.
Means of verification:	By design. Units testing. Systems testing. Acceptance tests
Dependencies:	NF_PR_03, NF_SP-02

Requirement ID:	**NF_SP_07**	Priority:	Mandatory
Requirement title:		GDPR Audit	
Description:		Platform will maintain a log of all operations performed upon personal data	
Rationale/Goal:		Security and privacy	
Means of verification:		Legal requirements testing	
Dependencies:		NF_LE_07	

Requirement ID:	**NF_SP_08**	Priority:	Mandatory
Requirement title:		Secure Authentication	
Description:		Registered end-user connecting to the platform must be authenticated via secure channels (HTTPS)	
Rationale/Goal:		Security and privacy	
Means of verification:		Units testing. Systems testing. Acceptance tests	
Dependencies:		NF_LE_03, NF_SP-09	

Requirement ID:	**NF_SP_09**	Priority:	**Optional**
Requirement title:		Physical Security (Data centers)	
Description:		Prevent unauthorised physical access and protect against theft, damage, and minimize loss of operations.	
Rationale/Goal:		Privacy and security	
Means of verification:		By design. System test. Security test.	
Dependencies:		NF_SP_02, NF_SP-08, NF_SP_10	

Requirement ID:	**NF_SP_10**	Priority:	Mandatory
Requirement title:		Operational Security	
Description:		Ensure proper and regular operation, including appropriate measures for continuous Security & Privacy Assurance tool monitoring of all RETENTION layers and components, to ensure best possible protection against malware, and security/privacy vulnerabilities and threats	
Rationale/Goal:		Security and privacy	
Means of verification:		By design. Systems tests. Acceptance tests.	
Dependencies:		NF_SP-02, NF_SP-09	

Requirement ID:	**NF_SP_11**	Priority:	Mandatory
Requirement title:		Securing personal data	
Description:		Ensure appropriate and effective use of cryptography to protect the confidentiality, authenticity or integrity of personal data been stored	
Rationale/Goal:		Security and privacy	
Means of verification:		By design. Unit testing. System testing. Regulatory and compliance.	
Dependencies:		NF_SP-07	

Requirement ID:	**NF_SP_12**	Priority:	Mandatory
Requirement title:		Incident management	
Description:		Ensure a consistent and comprehensive approach to the capture, assessment, communication and escalation of security/privacy incidents, and appropriate handling of government investigation requests for legal review, information to cloud customers, and limitation of access to or disclosure of data	
Rationale/Goal:		Security and privacy	
Means of verification:		By design. Unit testing. System testing. Continuous monitoring.	
Dependencies:		NF_SP_06, NF_SP_10	

6.6 Data and data exchange requirements

Requirement ID:	**NF_DE_01**	Priority:	**Mandatory**
Requirement title:		Data storage or exchange format	
Description:		Data storage/exchange format should respect the existing standards like HL7, or other predefined ones like JSON/CSV/XML/SQL Data Types or other common health data format	
Rationale/Goal:		Unify the structure of data to facilitate the data modelling step	
Means of verification:		By design.	
Dependencies:		NF_SP_04, NF_DE_02	

Requirement ID:	**NF_DE_02**	Priority:	**Mandatory**
Requirement title:		Data Exchange Protocol: transport	
Description:		Enhanced transport requirements should be Secure HTTP (HTTPS) for complex messages	

Rationale/Goal:	HTTPS consists of the standard HTTP layered on top of a secure Transport Level Security (TLS1.2 minimum required) session which ensures a secured communication
Means of verification:	Unit testing. Integration tests. System test. Acceptance test
Dependencies:	NF_DE_01, NF_SP_04

Requirement ID:	**NF_DE_03**	Priority:	**Optional**
Requirement title:		Data Exchange Protocol	
Description:		For lightweight messages we should use MQTT, or more secured similar protocols (like MQT-TZ)	
Rationale/Goal:		MQTT makes it easy to encrypt messages using TLS and authenticate clients using modern authentication protocols, such as OAuth.	
Means of verification:		Unit testing. Integration tests. System test.	
Dependencies:		NF_DE_01, NF_DE_02	

Requirement ID:	**NF_DE_04**	Priority:	Mandatory
Requirement title:		Data storage	
Description:		Data should be stored in a SQL/NoSQL timeseries database	
Rationale/Goal:		Easy to scale and access the required data	
Means of verification:		By design. Unit testing. Integration tests. System test.	
Dependencies:		NF_DE_01, NF_DE_05	

Requirement ID:	**NF_DE_05**	Priority**:**	Mandatory
Requirement title:		Encrypted data transmission	
Description:		Mobile App to transmit data via a secure HTTPS channel, while the Dashboard to provide authentication subject to Authorisation policy. Symmetric key encryption based on the Advanced Encryption Standard (AES-256) algorithm, or other based on the Secure Hash Algorithms family to be utilised.	
Rationale/Goal:		Even in case that connection is hacked, transmitted data is protected from reading	
Means of verification:		By design.	
Dependencies:		NF_DE_04	

6.7 RETENTION Global Insights Cloud

Requirement ID:	**NF_GIC_01**	Priority**:**	Mandatory

Requirement title:	Security: Passwords management
Description:	A System Administrator role will manage user roles and authorizations for the restricted access based on use roles
Rationale/Goal:	Every user has access to data and views based on his role
Means of verification:	Audit to user roles and assignments – Usability testing
Dependencies:	NF_SP_01, NF_SP_02

Requirement ID:	**NF_GIC_02**	Priority:	Mandatory
Requirement title:		Security: Secure data flow	
Description:		Data and intervention models flowing between GIC and CSB should be secured from attacks (e.g. 'man in the middle' type of attacks)	
Rationale/Goal:		Ensure that the system adequately satisfies the security requirements	
Means of verification:		Security testing	
Dependencies:		NF_GIC_01, NF_SP_01	

Requirement ID:	**NF_GIC_03**	Priority:	Mandatory
Requirement title:		Operational: GIC components interactions	
Description:		The GIC should expose an integration layer capable for exposing data and models between its components (e.g., through API interfaces, stream-processing bus etc).	
Rationale/Goal:		Seamless data flow between GIC components	
Means of verification:		Performance and usability testing	
Dependencies:		NF_GIC_01, NF_SP_10	

6.8 RETENTION Clinical Site Backend

Requirement ID:	**NF_CSB_01**	Priority:	Mandatory
Requirement title:		Security: Passwords management	
Description:		A System Administrator role will manage user roles and authorizations for the restricted access based on use roles	
Rationale/Goal:		Every user has access to data and views based on his role	
Means of verification:		Audit to user roles and assignments – Usability testing	
Dependencies:		NF_SP_01, NF_SP_02	

Requirement ID:	**NF_CSB_02**	Priority:	Mandatory
Requirement title:		Security: Secure data flow	
Description:		Data and intervention models flowing between CSB and GIC and between CSB and RETENTION Patient End should be secured from attacks (e.g. 'man in the middle' type of attacks)	
Rationale/Goal:		Ensure that the system adequately satisfies the security requirements	
Means of verification:		Security testing	
Dependencies:		NF_CSB_01, NF_SP_01	

6.9 RETENTION Patient Edge & Gateway and analytics

Requirement ID:	**NF_PE_01**	Priority:	Mandatory
Requirement title:		Patient edge always on	
Description:		The patient edge will be 99.5% ON, for the use of the patient and the carer	
Rationale/Goal:		For the patient to send measurements, the gateway must be always on	
Means of verification:		By design	
Dependencies:		NF_PE_03	

Requirement ID:	**NF_ PE _02**	Priority:	Mandatory
Requirement title:		Patient edge connectivity and protocols	
Description:		The edge gateway must provide all available protocols and connections for the devices in project	
Rationale/Goal:		To get all data form the patient or carer	
Means of verification:		By design	
Dependencies:		NF_PE_03	

Requirement ID:	**NF_ PE _03**	Priority:	Mandatory
Requirement title:		Patient edge API	
Description:		Simple and adequate API to communicate with external devices	
Rationale/Goal:		to be simple for a new device to get onboard	
Means of verification:		By design	
Dependencies:		NF_PE_02	

Requirement ID:	**NF_PE_04**	Priority:	optional
Requirement title:		Adequate streaming engine	
Description:		Adequate streaming capabilities for real time data, in volumes and speeds	
Rationale/Goal:		To be able to stream data in high volumes and speeds	
Means of verification:		By design	
Dependencies:		NF_PE_01	

Requirement ID:	**NF_PE_05**	Priority:	Mandatory
Requirement title:		Easy to integrate with AI, BI, DSS, other applications	
Description:		Easy to integrate with other applications, by following industry standards, like HL7.	
Rationale/Goal:		To be able to integrate with other applications	
Means of verification:		By design	
Dependencies:		NF_PE_01, NF_PE_02, NF_PE_03	

Requirement ID:	**NF_PE_06**	Priority:	Mandatory
Requirement title:		Full secure edge software	
Description:		Security for patient and carer data is of outmost importance, so the gateway must be able to operate under a security scheme (end to end encryption)	
Rationale/Goal:		To be able to work under a high security scheme	
Means of verification:		By design	
Dependencies:		NF_SP_01	

6.10 Scalability

Requirement ID:	**NF_SM_1**	**Priority:**	Mandatory
Requirement title:		Scalability	
Description:		Refers to the capability of the platform to scale-up or down the hardware resources in a dynamic manner in order to adjust the abovementioned to the requested workload changes, maximizing the use of resources.	
Rationale/Goal:		A cloud platform must be expandable in terms of hardware and software components.	
Means of verification:		By design	
Dependencies:		NF_SP_10	

Functional Requirements

6.11 Authentication & Authorization

Requirement ID:	**FN_AA_01**	Priority:	Mandatory
Requirement title:		Security – End-user registration	
Description:		1. An end-user of the platform might gain access to the RETENTION platform if he/she provides a valid email, full name, organization, role and a hard-to-guess password; CAPTCHA to determine whether the user fills mandatory fields is real or a spam robot; 2. An email notification containing a link is generated to validate the email sent upon registration completion. In order to proceed, the end-user should verify his/her email address using the specific link. 3. Upon successful validation, registration request will be subject to administrator approval. Administrator will contact a responsible for the specific organization (each RETENTION organization must nominate at least one "responsible person") to confirm the end-user's identity, role and email. Upon receiving and confirming the relevant information, enters the admin area to approve or deny the registration request. • Alternatively, already has a list of all the accepted end-users/roles per organization 4. An email notification is sent informing about the outcome (acceptance/rejection).	
Rationale/Goal:		End user registration	
Means of verification:		• Email with a unique link to validate the registered email; • Registration data is stored in the end-user account (encrypted); • Confirmation email is sent to the validated email address. System logs this transmission. o If end-user entered invalid data or chose to cancel the account creation request, no account record will be created.	
Dependencies:		NF_GIC_01, NF_CSB_01	

Requirement ID:	**FN_AA_02**	Priority	**Mandatory**
Requirement title:		Security – End-user login	
Description:		1. In order to login, the valid end-user should provide his/her email address and the password. 2. System checks credentials against the stored ones (e.g., compare the encrypted entered password with the stored hash) and	

	• upon successful match (login), logs the end-user in the Dashboard (home page); • displays an error message to the user and redirects to the login form. On the third failed attempt, CAPTCHA mechanism is activated.
Rationale/Goal:	User login
Means of verification:	• CAPTCHA to determine whether the user is real or a spam robot; • System logs all login attempts (email, IP, timestamp).
Dependencies:	FN_AA_01

Requirement ID:	**FN_AA_03**	Priority**:**	**Mandatory**
Requirement title:		Security - End-user logout	
Description:		1. The end-user logouts from his/her RETENTION platform account; 2. Upon successful log out, the system displays a success message to the end-user.	
Rationale/Goal:		logout	
Means of verification:		• System logs all logout attempts (email, IP, timestamp).	
Dependencies:		FN_AA_02	

Requirement ID:	**FN_AA_04**	Priority**:**	**Mandatory**
Requirement title:		Security: Modifying end-user's registration info	
Description:		1. Admin/end-user selects end-user registration record; • Admin is able to alter account status, and role; • End-user is able to alter his/her email, full name and role (to be approved); He/she can also change the account password. 2. Upon successful alternation, the system displays a message to the admin/end-user. 3. End-users are sent an email notification if they change or reset their email or/and password on their account. Password changed notifications are not sent if the end-user is in an inactive state.	
Rationale/Goal:		FN_AA_01, FN_AA_02	
Means of verification:		• System logs email or password attempts (email, IP, timestamp). • System logs informative email timestamp.	
Dependencies:		FN_AA_01 ,FN_AA_02	

Requirement ID:	**FN_AA_05**	Priority**:**	**Mandatory**
Requirement title:		Security/Privacy: Create a study participant (minimum personal) record	

Description:	Recruitment: patient (or study participant) is recruited for RETENTION, he/she goes to the local pilot partner and signs the consent form) 1. The patient is registered at the local clinical system of the pilot partner (outside RETENTION scope). An ID is associated with his/her medical record; 2. RETENTION patient record is created by a authorized end-user (e.g., CCM). During this process, system will create automatically a pseudo identifier (Pseudo-Id1) for the patient, while the external ID is also stored; • Alternatively, Pseudo-Id1 is stored withing the scope of the local clinical system. 3. When it creates Pseudo-Id1, the system will also create a second (internal) pseudo identifier (i.e., Pseudo-Id2) and associate it with Pseudo-Id1 simultaneously; 4. IDs association (i.e., between Pseudo-Id1 and Pseudo-Id2) is stored in encrypted fashion. This Pseudo-Id2 will be used by the RETENTION system onwards as the id for any data that will ever be received for the particular patient (e.g., via the app). The association will be used in data ingestion and extraction. Pseudo-Id2 will NOT be communicated outside from RETENTION system. 5. RETENTION patient record will contain the Pseudo-Id1, a randomly associated email (for enabling the smartphone's automated update mechanism), the clinical organisation has been associated with, the consent timestamp along with up to 3 clinical case manager(s) (valid RETENTION end-users) and up to 3 caregivers/close relatives (emails) that can be informed in case of an emergency (patient provides consent to do so). 6. Caregivers/close relatives are sent an email notification indicating that where they are informed in case of an emergency for a particular RETENTION study participant.
Rationale/Goal:	Security, privacy authorization, GDPR,
Means of verification:	• System logs viewing/editing attempts of personal information records been made (email, IP, timestamp). • System logs informative email timestamp.
Dependencies:	FN_AA_02

Requirement ID:	**FN_AA_06**	Priority:	**Mandatory**
Requirement title:		Security/Privacy: Alter study participant record	
Description:		1. An authorized end-user (e.g., CCM) alters, the randomly associated email, or the clinical organisation, or any of the associated clinical case manager(s)/ caregivers/close relatives.	

	2. Caregivers/close relatives are sent an email notification indicating that where they are informed in case of an emergency for a particular RETENTION study participant
Rationale/Goal:	Security/Privacy: Create a study participant (minimum personal) record
Means of verification:	• System logs viewing/editing attempts of personal information records been made (email, IP, timestamp). • System logs informative email timestamp.
Dependencies:	FN_AA_02, FN_AA_05

Requirement ID:	**FN_AA_07**	Priority:	Optional
Requirement title:		Privacy: GDPR requests management	
Description:		1. Patient through his/her smartphone or an authorised end-user(s) (e.g., pilot partner CCM who recruited him/her) through the Dashboard may initiate a GDPR request, stating the category and accompanying text if is deemed appropriate; 2. Upon the receipt of such a request, system administrator (and other if necessary) will proceed copying with the particular request; 3. Response (and relevant data in machine-readable format if applicable) will be delivered to patient's smartphone or the relevant clinical partner respectively.	
Rationale/Goal:		Security, privacy authorization, GDPR	
Means of verification:		• System logs GDPR request initiation and changes in its status.	
Dependencies:		NF_LE_05	

Requirement ID:	**FN_AA_08**	Priority:	**Optional**
Requirement title:		Privacy: Maintain records of processing activities	
Description:		Logging mechanism of GDPR requests tracks the progress of individual cases (i.e., participant's Id, requested-on behalf, status, request timestamp, time-limits, assigned-to, justification, completion timestamp (if any)) and demonstrates compliance with the GDPR (compliance with timescales, maintained logs for audit, evidence to be requested by the supervisory authority).	
Rationale/Goal:		Security, privacy authorization, GDPR	
Means of verification:		• System logs GDPR request initiation and changes in its status.	
Dependencies:		NF_LE_07	

Requirement ID:	FN_AA_09	Priority:	Mandatory
Requirement title:		Privacy: authorization levels	
Description:		The system will have full security with compartmentalized levels, with at least security for each level, security for the role and security for .	
Rationale/Goal:		Security, privacy and authorization	
Means of verification:		Unit test, system test, vulnerability test.	
Dependencies:		FN_AA_10, NF_SP_02	

Requirement ID:	FN_AA_10	Priority:	Mandatory
Requirement title:		Privacy: authorization system	
Description:		The system will have full security with compartmentalized levels, with at least security for each level, security for the role and security for all roles. At least with the following Roles: • Patients and carers • Clinicians • Statisticians/policy makers • Administrators. The administrators will accept the doctors, The clinicians will accept the patients and the carer	
Rationale/Goal:		Security, privacy and authorization	
Means of verification:		Unit test, system test, vulnerability test.	
Dependencies:		FN_AA_09, NF_SP_02	

6.12 Audit Tracking and Administrative

Requirement ID:	FN_TA_01	Priority:	Optional
Requirement title:		Audit tracking	
Description:		The system will have full audit tracking in all levels.	
Rationale/Goal:		Security, privacy authorization, GDPR	
Means of verification:		• System logs GDPR request initiation and changes in its status.	
Dependencies:		NF_SP_07	

6.13 Business rules: corrections, cancellations, and adjustments of transactions

Requirement ID:	FN_BT_01	Priority:	Mandatory
Requirement title:		corrections, cancellations, and adjustments of transactions	

Description:	All system corrections, cancellations, and adjustments of transactions will be monitored and can audited at any time
Rationale/Goal:	Business rules
Means of verification:	Unit test, system test, acceptance tests.
Dependencies:	FN_TA_01

6.14 Certification and Devices

Requirement ID:	**FN_CD_01**	Priority:	**Optional**
Requirement title:		Certifications	
Description:		Certifications as needed.	
Rationale/Goal:		System certifications	
Means of verification:		Legal requirements.	
Dependencies:		NF_LE_06	

6.15 Data and Reporting

Requirement ID:	**FN_DR_01**	Priority:	**Mandatory**
Requirement title:		Historical data	
Description:		Historical data will be maintained according to the GDPR rules	
Rationale/Goal:		History of the data in the system	
Means of verification:		By design and continuous monitoring.	
Dependencies:		NF_LE_05, NF_LE_07	

Requirement ID:	**FN_DR_02**	Priority:	**Mandatory**
Requirement title:		Reporting	
Description:		Historical data will be maintained according to the GDPR rules	
Rationale/Goal:		Reporting and GDPR compliance	
Means of verification:		Unit test. System test. Acceptance test.	
Dependencies:		FN_HR_01, NF_LE_05	

Requirement ID:	**FN_DR_03**	**Priority:**	**Mandatory**
Requirement title:		Data input frequency	
Description:		Data shall be provided at a regular interval and constantly fed into the Big Data analytics and models update platform.	
Rationale/Goal:		Constant data input frequency.	
Means of verification:		Add module that counts number of reports daily	

Dependencies:	NF_DR_02

Requirement ID:	**FN_DR_04**	**Priority:**	**Mandatory**
Requirement title:		Data mechanisms and processes.	
Description:		All processes and mechanisms for data cleaning, linking and merging various individual data, must be defined and implemented in an automated manner. Data cleaning process ensuring that invalid data are not considered.	
Rationale/Goal:		Interoperability layer: Prep data as input for AI models.	
Means of verification:		By design. Systems testing. Acceptance tests.	
Dependencies:		NF_DE_01	

6.16 External Interfaces

Requirement ID:	**FN_EI_01**	Priority:	**Optional**
Requirement title:		External interfaces	
Description:		The system will be able to connect to external systems if that will be required according to interoperability standards	
Rationale/Goal:		Connect to external systems	
Means of verification:		system testing	
Dependencies:		NF_DE_01, NF_DE_02	

6.17 Mobile Application

Requirement ID:	**FN_MA_01**	Priority:	**Mandatory**
Requirement title:		Secure Connect to the RETENTION system.	
Description:		when it starts up, the application connects automatically to the system, via secure channels. The mobile phone/tablet is registered to the systems to be accepted.	
Rationale/Goal:		AUTO-Connect to the RETENTION system.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		NF_SP_02	

Requirement ID:	**FN_MA_02**	Priority:	**Mandatory**
Requirement title:		User login	
Description:		The patient or carer can login to the RETENTION system via the mobile application	
Rationale/Goal:		Connect to the RETENTION system.	

Means of verification:	Unit testing. System testing. Integration testing.
Dependencies:	FN_MA_01

Requirement ID:	**FN_MA_03**	Priority:	**Mandatory**
Requirement title:		Wellness advanced report	
Description:		The patient or carer will be able to insert with ease the advanced report of the patient at the moment of use. The application will do this if the patient IS NOT feeling well (typical medical questions).	
Rationale/Goal:		Get the advanced wellness report from the patient or carer, when the patient is not feeling well.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_04**	Priority:	**Mandatory**
Requirement title:		CONNECT local (on the mobile device) or external devices (direct to the cloud).	
Description:		The patient or carer will be able to easily connect devices with compatible technology, to the phone/tablet and in extent to the mobile application and the RETENTION system. The application will be able to recognize the device and send/receive data. All new devices will be reported to RETENTION.	
Rationale/Goal:		Connect devices to the phone/tablet and in extension to the RETENTION system.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_BT_01, FN_MA_02	

Requirement ID:	**FN_MA_05**	Priority:	**Mandatory**
Requirement title:		Basic data capture from local (on the mobile device) connected devices.	
Description:		The patient or carer will be able to easily capture data from locally connected devices to the phone/tablet via protocols like Bluetooth or others. (Devices must already be connected to the phone/tablet and registered in the mobile application and in extension to the RETENTION system).	
Rationale/Goal:		Capture onboard data form devices.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02, FN_MA_03	

Requirement ID:	FN_MA_06	Priority:	Optional
Requirement title:		Extended data capture from external devices, NOT directly connected to the mobile device	
Description:		The patient or carer will be able easily connect devices to the mobile application that are external to thephone/tablet and mobile application. (Devices must already be connected to mobile application and registered in it and in extension to the RETENTION system.	
Rationale/Goal:		Capture data from external devices.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02, FN_MA_03	

Requirement ID:	FN_MA_07	Priority:	Mandatory
Requirement title:		Data visualization from devices.	
Description:		The patient or carer will be able easily visualize the data from the platform. Ex. for the oximeter, the mobile app will display the % of oxygen at the given time.	
Rationale/Goal:		Data visualization.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02, FN_MA_03	

Requirement ID:	FN_MA_08	Priority:	Mandatory
Requirement title:		Visualize the Electronic Health Record on system.	
Description:		The patient or carer will be able to easily visualize parts of Electronic Health Record kept by the RETENTION system.	
Rationale/Goal:		EHR Data visualization.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	FN_MA_09	Priority:	Mandatory
Requirement title:		Add or modify and submit questionnaires or surveys.	
Description:		The patient or carer will be able to easily add, modify and submit questionnaires and/or surveys given by the clinical teams.	
Rationale/Goal:		Add, edit and submit questionnaires ans surveys.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_10**	Priority:	**Mandatory**
Requirement title:		Panic or problem alert.	
Description:		The patient or carer will be able to easily alert the medical team for a PANIC or DANGEROUS condition.	
Rationale/Goal:		Panic and/or dangerous condition alert to the medical team.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_11**	Priority:	**Mandatory**
Requirement title:		TEXT Messaging system that connects to the medical team.	
Description:		The patient or carer will be able to easily send a TEXT message to the medical team (NOT emergency).	
Rationale/Goal:		Messaging the clinical team for advice and information. On NON-dangerous conditions.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_12**	Priority:	**Mandatory**
Requirement title:		chat system that connects to the medical team.	
Description:		The patient or carer will be able to easily live chat with the medical team.	
Rationale/Goal:		Chat with the clinical team for advice and information.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_13**	Priority:	M**andatory**
Requirement title:		chat system with photograph send support	
Description:		The patient or carer will be able to send photos to the medical team.	
Rationale/Goal:		Inform medical team with photos	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_14**	Priority:	**Mandatory**
Requirement title:		Adherence to therapy.	
Description:		The patient (or via the carer) will be monitored for the patient's adherence to treatment (taking his medication timely and correctly) .	
Rationale/Goal:		Patient adherence to treatment.	

Means of verification:	Unit testing. System testing. Integration testing.
Dependencies:	FN_MA_02

Requirement ID:	**FN_MA_15**	Priority:	**Mandatory**
Requirement title:		Integration and visualization of external services data	
Description:		the system will integrate and visualize external data, such as pollution, temperature and others.	
Rationale/Goal:		Integration of External services data.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_16**	Priority:	**Mandatory**
Requirement title:		Automated system messages	
Description:		the mobile application will receive automate system messages from the RETENTION AI or DSS and pass them to the patient or carer.	
Rationale/Goal:		To receive automated system messages.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_17**	Priority:	**Mandatory**
Requirement title:		Manual system messages (via the clinical team)	
Description:		the mobile application will receive manual system messages (via the clinical team), generated by the clinical team, down to the patient or carer.	
Rationale/Goal:		To receive messages from the clinical team.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02	

Requirement ID:	**FN_MA_18**	Priority:	**Mandatory**
Requirement title:		Personalization of data and interface	
Description:		the mobile application will adapt the behavior and visualization	
Rationale/Goal:		Personalized interface.	
Means of verification:		Unit testing. System testing. Integration testing.	
Dependencies:		FN_MA_02, NF_US_03	

6.18 Dashboard Interactions

Requirement ID:	**FN_DI_01**	Priority:	**Mandatory**

Requirement title:	CSB: Access to specific patient variables
Description:	Clinicians need to have access to full insights and variable knowledge of each patient and all types of variables should be presented in a clear and understandable way
Rationale/Goal:	Clear clinical view of patient
Means of verification:	System testing
Dependencies:	NF_CSB_01

Requirement ID:	**FN_DI_02**	Priority:	**Mandatory**
Requirement title:		CSB: Store patient's visit data	
Description:		Clinicians have to be able to enter and store information during a patients visit from a predefined list of actions	
Rationale/Goal:		Update system data after patient's visit	
Means of verification:		System testing	
Dependencies:		FN_DI_01	

Requirement ID:	**FN_DI_03**	Priority:	**Mandatory**
Requirement title:		CSB: Chat functionality	
Description:		Clinicians have to be able to be informed about chat interaction or patients message request in a convenient way	
Rationale/Goal:		Not miss chat message between clinician and patient/care giver	
Means of verification:		System testing	
Dependencies:		FN_MA_12	

Requirement ID:	**FN_DI_04**	Priority:	**Mandatory**
Requirement title:		CSB: Validation of proposed intervention	
Description:		Retention dashboard will display the proposed intervention to clinician for specific patient that it should be accepted by the clinician	
Rationale/Goal:		Approved and validated interventions	
Means of verification:		System testing	
Dependencies:		FN_DI_01	

Requirement ID:	**FN_DI_05**	Priority:	**Mandatory**
Requirement title:		CSB: Alarm/Notification creation	
Description:		The clinician approves an intervention and the system creates the relative notification on patient's device	
Rationale/Goal:		Approved and validated notifications	
Means of verification:		System testing	

Dependencies:	FN_DI_04

Requirement ID:	**FN_DI_06**	Priority:	**Mandatory**
Requirement title:		CSB: Special events notification	
Description:		The visualization provides a notification area in order the clinician to be informed about special events triggered by patient/care giver	
Rationale/Goal:		Communication of special events	
Means of verification:		System testing	
Dependencies:		FN_MA_10	

Requirement ID:	**FN_DI_07**	Priority:	**Mandatory**
Requirement title:		CSB: Device management for activation/deactivation	
Description:		The clinician can assign a specific monitoring device to a patient after her enrollment. Also, she can deactivate this device if needed	
Rationale/Goal:		Association of a device to specific patient	
Means of verification:		System testing	
Dependencies:		FN_MA_04	

Requirement ID:	**FN_DI_08**	Priority:	**Mandatory**
Requirement title:		GIC: Models transfer from GIC to CSB	
Description:		The data analyst should be able to validate an intervention model to be used in CSB interventions	
Rationale/Goal:		Model trained in GIC to be executed in CBS intervention models execution environment	
Means of verification:		System testing	
Dependencies:		FN_GIC_02	

Requirement ID:	**FN_DI_09**	Priority:	**Mandatory**
Requirement title:		GIC: Identification of new parameters	
Description:		The data analyst should be informed about new parameters identified as a result of data analysis	
Rationale/Goal:		New/updated models	
Means of verification:		System testing	
Dependencies:		FN_DI_10	

Requirement ID:	**FN_DI_10**	Priority:	**Mandatory**
Requirement title:		GIC: Data analysis for research purposes	

Description:	A data analyst / researcher can perform statistical analysis of the available data and the system provides a set of predefined functions and visualization widgets
Rationale/Goal:	Statistical analysis of available data for research purposes
Means of verification:	System testing
Dependencies:	FN_DI_09

Requirement ID:	**FN_DI_11**	Priority:	**Optional**
Requirement title:		GIC: GDPR and audit check	
Description:		An auditor should have access to all GDPR and audit check requests with detailed info regarding the status of the completion process and the persons involved	
Rationale/Goal:		Facilitation of audit check	
Means of verification:		System testing	
Dependencies:		NF_LE_05, NF_SP_07	

Requirement ID:	**FN_DI_12**	Priority:	**Mandatory**
Requirement title:		GIC: Patients' devices configuration	
Description:		The system administrator has to be able to apply pseudo-anonymized IDs of patients' devices, facilitating their configuration	
Rationale/Goal:		Patient's devices configuration	
Means of verification:		System testing	
Dependencies:		NF_LE_05	

6.19 The top level BI-AI, Big Data, applications

AI (Artificial Intelligence) / ML (Machine Learning):

Requirement ID:	**FN_BIAI_01**	Priority:	**Mandatory**
Requirement title:		AI Models Build and Deploy	
Description:		The top-level layer will support the creation and editing of AI models and the components needed to execute the analytics, the DSSs and support the clinical interventions.	
Rationale/Goal:		AI design and development for risk/status prediction	
Means of verification:		Perform technical tests, model performance	
Dependencies:		FN_BIAI_03	

Requirement ID:	**FN_BIAI_02**	Priority:	**Mandatory**
Requirement title:		Serialized AI models	
Description:		The AI should produce serializable model outcomes. In the serialized form, the data can be delivered to another data store, application, or other destination.	

Rationale/Goal:	Serialization for an easily transmittable form.
Means of verification:	Build a test unit for transmitting and deserializing models
Dependencies:	FN_BIAI_01

Requirement ID:	**FN_BIAI_03**	Priority:	**Mandatory**
Requirement title:		AI models and analytics input data	
Description:		The input data for AI models should be structured files, such as JSON, CSV files. The imported data within the Gateway should have a hierarchical structure, such as JSON/XML format.	
Rationale/Goal:		Input data.	
Means of verification:		By design.	
Dependencies:		FN_BIAI_01, FN_BIAI_09	

Requirement ID:	**FN_BIAI_04**	Priority:	**Optional**
Requirement title:		Use efficient models	
Description:		AI Models should be optimized such as not to be computational expensive.	
Rationale/Goal:		Efficiency of the computational costs.	
Means of verification:		Compare training times versus prediction accuracy	
Dependencies:		FN_BIAI_01	

Requirement ID:	**FN_BIAI_05**	Priority:	**Mandatory**
Requirement title:		Trustworthiness of models	
Description:		Models should be, verifiable and trustworthy.	
Rationale/Goal:		Offering and verifiable decision-making capabilities that leverage the evidence produced by the underlying data analysis and augment clinical studies targeting HF and other CVDs.	
Means of verification:		Present results in meetings and validate with other technical partners	
Dependencies:		n/a	

Big Data Platform:

Requirement ID:	**FN_BIAI_06**	Priority:	**Mandatory**
Requirement title:		Data structure	
Description:		Data should be easy to be retrieved and easy to be integrated within AI, BI, DSS and other applications, for example able to be retrieved easy and fast, in e.g., a tabular form (data frame).	
Rationale/Goal:		Data should be easy to read and interpret.	

Means of verification:	Testing.
Dependencies:	FN_BIAI_07, FN_BIAI_09

Requirement ID:	**FN_BIAI_07**	Priority:	**Optional**
Requirement title:		Data structure type	
Description:		Data should be homogeneous for an efficient processing, meaning same data structure across clinical centers	
Rationale/Goal:		Input data.	
Means of verification:		Acceptance Testing.	
Dependencies:		FN_BIAI_06	

Requirement ID:	**FN_BIAI_09**	Priority:	**Mandatory**
Requirement title:		FAIR	
Description:		Data should respect FAIR principles, such as findable, accessible, interoperable, reusable	
Rationale/Goal:		By respecting the FAIR principles data can be easily used by the RETENTION framework	
Means of verification:		Certified by technical partners	
Dependencies:		FN_BIAI_03, FN_BIAI_06	

Requirement ID:	**FN_BIAI_09**	Priority:	**Mandatory**
Requirement title:		Get metadata of a data base schema	
Description:		The Big Data Platform should access a REST functionality to enable the retrieval of information regarding a DB schema. This will allow to retrieve the list of corresponding tables/indices, the tables' column names and data types, the primary/foreign key constraints.	
Rationale/Goal:		Data Visualization Dashboard.	
Means of verification:		Querying database tables/indices of interest	
Dependencies:		FN_BIAI_10	

Requirement ID:	**FN_BIAI_10**	Priority:	**Mandatory**
Requirement title:		API access to data	
Description:		Big Data Platform should access a REST functionality to allow the Data Analytics components to retrieve intermediate query results of their execution	
Rationale/Goal:		Real-time access to data	
Means of verification:		Querying the provided REST API	
Dependencies:		FN_BIAI_06	

BI (Business Intelligence) / Analytics:

Requirement ID:	**FN_BIAI_11**	Priority:	**Mandatory**
Requirement title:		AI Design	
Description:		With respect to HF management, including prediction and progression, the goal is to investigate patient features and how they correlate with outcomes, providing the means for key factors identifications that affect patient health status. This can be achieved through a combination of classification, process mining and pattern mining techniques, and visual analytics.	
Rationale/Goal:		Build models to diagnose based on certain KPIs read from the patient	
Means of verification:		Validate by clinician	
Dependencies:		FN_BIAI_01	

Requirement ID:	**FN_BIAI_12**	Priority:	**Mandatory**
Requirement title:		Big Data Processing	
Description:		AI models and analytics should be able to handle big amounts of data well.	
Rationale/Goal:		Capability to work with large amount of data	
Means of verification:		By testing	
Dependencies:		FN_BIAI_011	

Requirement ID:	**FN_BIAI_13**	Priority:	**Mandatory**
Requirement title:		Validate data	
Description:		Input data for AI models and BI/Analytics should be consistent, as complete as possible, unique (no duplicates), and the data must be accurate to correctly represent the recorded events (no missing timestamp or measurement information).	
Rationale/Goal:		Filter out redundant data	
Means of verification:		Build a validation system for these types of scenarios	
Dependencies:		FN_BIAI_03	

Requirement ID:	**FN_BIAI_14**	**Priority:**	**Mandatory**
Requirement title:		Alert System	
Description:		AI models results and analytics should support corresponding alerts necessary towards the clinical level.	
Rationale/Goal:		Build an alert decision support systems with multiple alert levels	
Means of verification:		Validate by clinician	
Dependencies:		FN_DI_05	

Requirement ID:	FN_BIAI_15	**Priority:**	Optional
Requirement title:		Recurring update of models	
Description:		AI models should be generated/updated on a regular interval. Once new data is added into system, the models need to take that into consideration	
Rationale/Goal:		Update models regularly with new data. Raise alert if a model stagnates	
Means of verification:		By design	
Dependencies:		FN_DI_04	

Requirement ID:	**FN_BIAI_16**	Priority:	**Mandatory**
Requirement title:		Causal analysis through monitoring of policies' KPIs.	
Description:		KPIs monitoring is essential in the assessment or development of health policies. In this context, causal analysis refers to the association of potential changes in specific KPIs with certain interventions or with other available patient related data. Such associations can facilitate the identification of factors that influence policy impact. A KPI monitoring dashboard is required for this process, available for public health experts.	
Rationale/Goal:		Help improving existing policies	
Means of verification:		Validate by clinician	
Dependencies:		FN_BIAI_17	

Requirement ID:	**FN_BIAI_17**	Priority:	**Mandatory**
Requirement title:		Conceptual analysis of policies' KPIs.	
Description:		conceptual framework for the KPIs and their relationships could help in the design of public health policies. Public health experts will assess the final evaluation of the policies based on the given evidence. The outcome can be in the form of acceptance/non-acceptance along with recommendations for improvement.	
Rationale/Goal:		Policy analysis and evaluation	
Means of verification:		Validate by clinician	
Dependencies:		FN_BIAI_16	

Applications:

Requirement ID:	**FN_BIAI_18**	Priority:	**Mandatory**
Requirement title:		Data and model sharing	
Description:		AI & BI models should provide an open data sharing specification and model which will enable new partners to leverage RETENTION platform, bringing new clinical	

	trial data, new AI algorithms, as well as new types of smart devices into the platform, and linking it to additional domains and relevant piloting activities.
Rationale/Goal:	Exploit the validated RETENTION intervention and decision-making models in pertinent applications.
Means of verification:	Evaluate using feedback formulars
Dependencies:	FN_BIAI_11

7 Conclusions

The current deliverable reports the work performed by the participating partners during the lifecycle of Tasks 3.1 & 3.2. Analysis of the state of-the-of art for Heart Failure patient monitoring, both from clinical and technological perspective performed, as well as the trends in current clinical practice. Clinical study characteristics and the related risk factors were outlined, also including a detailed list of variables based on clinical practice and state-of-art research that should be monitored, the frequency when they will be monitored, and other provided functionalities described. This document provides the initial set of RETENTION requirements. A user requirement elicitation process was followed by the participating partners, after defining the users and stakeholders according to the current clinical practice and the above-mentioned state of the art about telemonitoring in HF. The information gathered was the basis for the preparation of questionnaires. Through the dedicated questionnaires and interviews the user needs were identified. Requirements were collected in terms of functionalities, usability, performance, availability, and reliability, legal and ethical, security and privacy, data and data exchange and scalability. Obtaining the user requirements is the first step which is needed for designing the RETENTION platform architecture. Those requirements are translated into non-functional and functional requirements of the RETENTION platform. Based on the user requirements, a range of different use cases and scenarios are described. This approach provides the opportunity for the end-users to describe how they conceive the use of the platform. The outcome of this process is summarised in the Sections 5 and 6, where all the requirements and usage scenarios are given.

In conclusion, this deliverable gave us the understanding of the RETENTION system, as seen from the point of view of the clinicians and the system users, focusing on the requirements that the patients, the caregivers the doctors, and the IT Managers. The state of the art either on clinical or on technical part, along with the innovative research, both in clinical and patient-carers, the clinical use case scenarios and the procedures on technical requirements gave enough knowledge to support the next deliverable on platform architecture.

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Appendix

Appendix 9.1: Questionnaires

PATIENT'S QUESTIONNAIRE

Dear Patient,

You have been recruited for an important study in patient monitoring. Your medical team is currently participating in a project that is trying to develop a platform to monitor patient's health and would like to ask your opinion about some aspects. The information will be very important for your health and the health of others in the future. Please take 3-5 minutes from your precious time to fill out this questionnaire.

Thank you.

What is the Retention project?

Retention is a project to develop and deliver an innovative platform supporting enhanced clinical monitoring and interventions aimed at improving the clinical management of patients with chronic heart failure (HF), reducing their mortality and hospitalization rates, and improving their quality of life, safety, and well-being. The RETENTION platform will support clinical decision making and evidenced based personalized interventions for HF patients by:

(a) continually monitoring and collecting medical, clinical, physiological, behavioural, psychosocial, and real-world data for such patients,

(b) analysing these data using innovative model-driven big data analytics, statistical, artificial intelligence, and machine learning techniques,

(c) detecting patterns in the HF disease progression and the quality of life of patients,

(d) cross checking and validating them against the clinical literature,

(e) offering transparent, explainable, and verifiable decision-making capabilities that leverage the evidence produced by the underlying data analysis and augment clinical studies targeting HF and other CVDs.

The RETENTION approach and its platform will be validated through a clinical study, involving a total of 450 HF patients recruited by 6 different hospitals in 4 different EU countries within which there is some diversity in the management of such patients

Data utilization

Data collected by your participation will be used exclusively for research purposes related to this study, following the rules established by the European and National legislation about data protection. From the data obtained from the questionnaires, information will be generated and included in D3.1 deliverable of the RETENTION project. It could be also used for educational purposes and scientific knowledge's dissemination.

Consent Form

Dear xxxx,

You are invited to participate in a survey on Heart Failure remote monitoring. This is a research project being conducted by (Name of the Hospital) with a European grant (No. 965343). It should take approximately 3-5 minutes to complete.

Submission of the survey will be interpreted as your informed consent to participate and that you affirm that you are at least 18 years of age.

PARTICIPATION
Your participation in this survey is voluntary. You may refuse to take part in the survey at any time without penalty. You are free to decline to answer any question you do not wish to answer for any reason. Participation or nonparticipation will not impact your relationship with your hospital or Health services.

BENEFITS
You will receive no direct benefits from participating in this research study. However, your responses may help us to design a remote monitoring platform for heart failure patients.

RISKS

There is the risk that you may find some of the questions to be sensitive. You are free to decline to answer any particular question you do not wish to answer for any reason.

CONFIDENTIALITY
Your survey answers will be stored in a password protected electronic format. This survey does not collect identifying information such as your name, address, or other personal information. Therefore, your responses will remain anonymous. No one will be able to identify you or your answers, and no one will know whether or not you participated in the survey.

CONTACT

If you have questions at any time about the study or the procedures, you may contact [name of clinical partner], via phone at [number] or via email at [email address].

If you feel you have not been treated according to the descriptions in this form, or that your rights as a participant in a survey have not been honoured during the course of this project, or you have any questions, concerns, or complaints that you wish to address to someone other than the investigator, you may contact with Christina Nanou via e-mail at christina.nanou@eunomia.ltd, who oversees this project's ethics and privacy related issues.

Personal information

1. Please select your age group:

a) < 40 years old

b) 40-60 years old

c) 60-70 years old

d) 70 years old

2. Please select your sex:

a) Male

b) Female

c) Other

3. Please, select your country

a) Germany

b) Greece

c) Italy

d) Spain

4. What is your education level?

a) Grammar school

b) High School

c) College degree,

d) Master's or Ph.D.

5. Are you currently working?

a) Yes

b) I am on medical leave

c) I am retired

6. Please select which of the following best represents your current health situation:

a) Heart failure patient

b) LVAD patient, whether enlisted or not for heart transplant

c) Heart transplant patient

Technology and health

7. What type of mobile phone do you have?

a) I don't have a phone.

b) Previous generation – non smart phone

c) Lite smartphone (less than 200 Euro)

d) Heavy duty smart phone (> 200 euro)

8. Select your internet connection at home:

a) I don't have an internet connection.

b) I have a slow internet connection (first generation DSL)

c) I have a fast internet connection (second generation DSL or VDSL)

9. Have you ever used a personal computer (PC)?

a) Yes

b) No

10. How would you rate your e-skills?

a) I don't have any idea about what you are talking about

b) I use a PC or other device for the internet

c) I use my PC or device with applications (like word, excel, etc)

11. What do you use your mobile phone for?

a) I don´t have my own mobile phone

b) for calls and messages only

c) calls, messages, social media/surfing the internet, running apps

12. When you search the internet about your health, what type of web sites do you look for? (You can select more than one)

a) I don't use Internet for health-related questions

b) Medical and/or patient forums

c) Health databases

d) Health portals

e) Scientific articles

Retention solution

13. If your doctor recommends it, would you use a mobile app or web application to control your health status?

1 (totally disagree)	2	3	4	5 (totally agree)

14. Have you ever used a digital health device? (Measuring Heart rate, blood pressure, oxygen saturation, etc)

a) Yes, once or twice
b) Yes, I use them often
c) No

15. Would you be willing to wear a device (such as a wristwatch) that would monitor some of your health parameters, such as pulse, daily activity, etc.?

1 (totally disagree)	2	3	4	5 (totally agree)

16. If we grant you a screen device to introduce some of your health information, which do you prefer?

a) Smartphone

b) Tablet

c) none

17. What functionalities would you like to have on this device? (Please select as many as you wish)

a) Chat with other patients

b) Chat with a clinician

c) Videochat with a clinician

d) Medication reminders

e) Medical visits reminders

f) Vitals checking (Weight, blood pressure and heart rate records, etc)

g) Alerts to the doctor in case of some of your health parameters are altered.

h) Educational material (nutrition, physical exercise…)

i) Measurement of sleep: deep and light sleep phases, sleep interruptions.

j) Measurement of daily activity: steps, distance, calories, floors climbed

18. Could you rank the following device characteristics according to how important they are to you?

	Not important	Slightly important	Moderately important	Important	Very important

Chat with other patients					
Chat with a clinician					
Videochat with a clinician					
Medication reminders					
Medical visits reminders					
Vitals checking (Weight, blood pressure and heart rate records, etc)					
Alerts to the doctor in case of altered parameters					
Educational material (nutrition, physical exercise…)					
Measurement of sleep: deep and light sleep phases, sleep interruptions.					
Measurement of daily activity: steps, distance, calories, floors climbed					

19. If the platform has educational content about nutrition, physical exercise, prevention of heart failure decompensations, etc., which format would you prefer?

a) Written content

b) short videos

c) I am not interested in educational material

20. How much would you agree to have a plug-in device at home that would collect information on sunlight, humidity, and pollution?

1 (totally disagree)	2	3	4	5 (totally agree)

21. Would you be willing to perform a 15-minute questionnaire on symptoms or quality of life? If so, on what basis?

a) No, I wouldn't
b) Yes, every 15 days.
c) Yes, monthly.
d) Only once

22. How much time per day would you be willing to spend on a platform (or mobile app) to monitor your health?

a) I would not like to use such device
b) Less than 5 minutes
c) 5-10 min
d) 10-20 min
e) >20 min
f) Whatever it needs following the doctor's instructions

23. Which of the following measurements would you be willing to perform daily?

	1 (totally disagree)	2	3	4	5 (totally agree)
Blood pressure					
Pulsioxymetry					
Weight					

Heart rate					
Liquid's intake					
Diuresis					
Nutrition intake					
Pills intake					
Your health status					
Whichever instructed by the doctors					

24. Would you prefer to maintain (store) some of the information in the platform private, non-available for your doctor?

a) Yes

b) No

25. If you have answer yes to the last question, please develop what information:

26. Would you like to receive warnings and recommendations from your doctor if altered parameters are detected?

a) Yes

b) No

c) Important warnings only

27. How much would you agree to give consent to this virtual platform to connect to your medical records at the hospital, so that we could more easily obtain information on your laboratory tests results, out-patient visits, etc.?

1 (totally disagree)	2	3	4	5 (totally agree)

28. Would you need your caregiver/companion to help you with the platform (or mobile app)?

a) Yes

b) No

29. How much would you like your caregiver/companion to have an active role (filling questionnaires, having access to educational material, medical visits reminders, etc) in the platform?

1 (totally disagree)	2	3	4	5 (totally agree)

30. if need be, would you be willing to manually insert information to the platform (or application) on the device or the internet?

a) Important stuff only (1 or 2 parameters)

b) Yes, but no more than 4 parameters.

c) Yes, but no more than 8 parameters.

d) No

CARER'S QUESTIONNAIRE

Dear carer:

You have been recruited for a very important study in patient monitoring. Your medical team is currently participating in a project that is trying to develop a platform to monitor patient's health and would like to ask your opinion about some aspects. The information will be very important for the health of others in the future. Please take 3-5 minutes from your precious time to fill out this questionnaire.

Thank you.

What is the Retention project?

Retention is a project to develop and deliver an innovative platform supporting enhanced clinical monitoring and interventions aimed at improving the clinical management of patients with chronic heart failure (HF), reducing their mortality and hospitalization rates, and improving their quality of life, safety, and well-being. The RETENTION platform will support clinical decision making and evidenced based personalized interventions for HF patients by:

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(g) analysing these data using innovative model-driven big data analytics, statistical, artificial intelligence, and machine learning techniques,

(h) detecting patterns in the HF disease progression and the quality of life of patients,

(i) cross checking and validating them against the clinical literature,

(j) offering transparent, explainable, and verifiable decision-making capabilities that leverage the evidence produced by the underlying data analysis and augment clinical studies targeting HF and other CVDs.

The RETENTION approach and its platform will be validated through a clinical study, involving a total of 450 HF patients recruited by 6 different hospitals in 4 different EU countries within which there is some diversity in the management of such patients

Data utilization

Data collected by your participation will be used exclusively for research purposes related to this study, following the rules established by the European and National legislation about data protection. From the data obtained from the questionnaires, information will be generated and included in D3.1 deliverable of the RETENTION project. It could be also used for educational purposes and scientific knowledge's dissemination.

Consent Form

Dear xxxx,

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Submission of the survey will be interpreted as your informed consent to participate and that you affirm that you are at least 18 years of age.

PARTICIPATION
Your participation in this survey is voluntary. You may refuse to take part in the survey at any time without penalty. You are free to decline to answer any particular question you do not wish to answer for any reason. Participation or nonparticipation will not impact your relationship with your Hospital or Health services.

BENEFITS
You will receive no direct benefits from participating in this research study. However, your responses may help us to design a remote monitoring platform for heart failure patients.

RISKS

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CONTACT
If you have questions at any time about the study or the procedures, you may contact with [name of clinical partner], via phone at [number] or via email at [email address].

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Personal information

1. Please select your age group:

e) < 40 years old

f) 40-60 years old

g) 60-70 years old

h) 70 years old

2. Please select your sex:

d) Male

e) Female

f) Other

3. Please, select your country

e) Germany

f) Greece

g) Italy

h) Spain

4. What is your education level?

e) Grammar school

f) High School

g) College degree,

h) Master's or Ph.D.

5. Are you currently working?

d) Yes

e) I am a professional carer

f) I am retired

g) I have a leave of absence to care for a patient

6. Please select which of the following best represents the person you take care of:

a) Heart failure patient

b) LVAD patient, whether enlisted or not for heart transplant

c) Heart transplant patient

Technology and health

7. What type of mobile phone do you have?

e) I don't have a phone.

f) Previous generation – non smart phone

g) Lite smartphone (less than 200 Euro)

h) Heavy duty smart phone (> 200 euro)

8. select your internet connection at home:

d) I don't have an internet connection.

e) I have a slow internet connection (first generation DSL)

f) I have a fast internet connection (second generation DSL or VDSL)

9. Have you ever used a personal computer (PC)?

c) Yes

d) No

10. How would you rate your e-skills?

d) I don’t have any idea about what you are talking about

e) I use a PC or other device for the internet

f) I use my PC or device with applications (like word, excel, etc)

11. What do you use your mobile phone for?

d) I don´t have my own mobile phone

e) for calls and messages only

f) calls, messages, social media/surfing the internet, running apps

12. When you search the internet about your health or your loved ones health, what type of web sites do you look for? (you can select more than one)

f) I don’t use Internet for health-related questions

g) Medical and/or patient forums

h) Health databases

i) Health portals

j) Scientific articles

Relationship with the patient

13. Describe your relationship with the patient

a) Husband/wife

b) Son/daughter

c) Brother/sister

d) Other relative

e) Professional caregiver

14. Are you the main carer?

a) Yes

b) No

15. How much time per day do you spend on patient care?

a) None, the patient is completely independent

b) 1 hour

c) 1-4 hour

d) 4-8 hour

e) Full time, the patient is completely dependent

16. Do you assist the patient with medication adherence?

a) No

b) I put her/his pills in a pill box every week

c) I give her/his pills everyday

RETENTION solution

17. In your opinion, do you believe that the patient is able to use a smartphone/device to collect data related to his/ her health?

a) Yes

b) Yes, but he/she will need some help

c) No

18. Would you be willing to help the patient to collect health data on a mobile app?

1 (totally disagree)	2	3	4	5 (totally agree)

19. If the doctor recommends it, would you be willing provide your own data to the mobile app

1 (totally disagree)	2	3	4	5 (totally agree)

20. If we give you a screen device to introduce some of the patient's health information, which would you prefer?

a) Smartphone

b) Tablet

21. What functionalities would you like to have on this device? (please select as many as you wish)

a) Chat with other carers

b) Chat with a clinician

c) Videochat with a clinician

d) Medication reminders

e) Medical visits reminders

f) Weight, blood pressure and heart rate records

g) Alerts to the doctor in case of altered parameters

h) Educational material (nutrition, physical exercise…)

22. Could you rank the following device characteristics according to how important they are to you?

	Not important	Slightly important	Moderately important	Important	Very important
Chat with other carers					
Chat with a clinician					
Videochat with a clinician					
Medication reminders					
Medical visits reminders					

Statistics to track your weight, blood pressure and heart rate records.					
Alerts to the doctor in case of altered parameters					
Educational material (nutrition, physical exercise…)					
Measurement of sleep: deep and light sleep phases, sleep interruptions.					
Measurement of daily activity: steps, distance, calories, floors climbed					

23. How much would you agree to have a plug-in device at home that would collect information on sunlight, humidity, and pollution?

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24. If the platform has educational content about nutrition, physical exercise, prevention of heart failure decompensations, stress management etc., which format would you prefer?

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27. Would you like to receive warnings and recommendations from the doctor if altered parameters are detected?

a) Yes

b) No

c) Important warnings only

28. How much would you like to have an active role (filling questionnaires, having access to educational material, medical visits reminders, etc) in the platform?

1 (totally disagree)	2	3	4	5 (totally agree)

CLINICIAN QUESTIONNAIRE

Thank you for taking some time to fill in this questionnaire. We are currently participating in a project that is trying to develop a platform to monitor patient's health in heart failure patients, and would like to ask your opinion about some aspects.

What is the Retention project?

Retention is a project to develop and deliver an innovative platform supporting enhanced clinical monitoring and interventions aimed at improving the clinical management of patients with chronic heart failure (HF), reducing their mortality and hospitalization rates, and improving their quality of life, safety, and well-being. The RETENTION platform will support clinical decision making and evidenced based personalized interventions for HF patients by:

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(l) analysing these data using innovative model-driven big data analytics, statistical, artificial intelligence, and machine learning techniques,

(m) detecting patterns in the HF disease progression and the quality of life of patients,

(n) cross checking and validating them against the clinical literature,

(o) offering transparent, explainable, and verifiable decision-making capabilities that leverage the evidence produced by the underlying data analysis and augment clinical studies targeting HF and other CVDs.

The RETENTION approach and its platform will be validated through a clinical study, involving a total of 450 HF patients recruited by 6 different hospitals in 4 different EU countries within which there is some diversity in the management of such patients

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Your participation in this survey is voluntary. You may refuse to take part in the survey at any time without penalty. You are free to decline to answer any particular question you do not wish to answer for any reason.

BENEFITS
You will receive no direct benefits from participating in this research study. However, your responses may help us to design a remote monitoring platform for heart failure patients.

RISKS

There is the risk that you may find some of the questions to be sensitive. You are free to decline to answer any particular question you do not wish to answer for any reason.

CONFIDENTIALITY
Your survey answers will be stored in a password protected electronic format. This survey does not collect identifying information such as your name, address or other personal information. Therefore, your responses will remain anonymous. No one will be able to identify you or your answers, and no one will know whether or not you participated in the survey.

CONTACT
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If you feel you have not been treated according to the descriptions in this form, or that your rights as a participant in a survey have not been honoured during the course of this project, or you have any questions, concerns, or complaints that you wish to address to someone other than the investigator, you may contact with Christina Nanou via e-mail at christina.nanou@eunomia.ltd, who oversees this project's ethics and privacy related issues.

Personal information:

1. Please select your age group:

i) 25-30 years old
j) 30-40 years old
k) 40-50 years old
l) 50-60
m) More than 60 years old

2. Please select your sex:

g) Male
h) Female
i) Other

3. Please, select your country

i) Germany
j) Greece
k) Italy
l) Spain

4. Select your background education

a) doctor

b) nurse

c) other, specify_____

5. How long have you been practicing your profession?

i) 0-5 years

j) 5-10 years

k) 10-15 years

l) 15-20 years

m) More than 20 years

Working environment and practice

6. Please select which of the following best represents your patient's situation (you can choose more than one):

d) Heart failure patient

e) LVAD patient, whether enlisted or not for heart transplant

f) Heart transplant patient

7. Have you got previous experiences with remote monitoring in heart failure patients?

a) Yes

b) No

8. Do you think that a specifically designed app can improve the follow-up of patients with heart failure?

1 (totally disagree)	2	3	4	5 (totally agree)

9. Do you use remote monitoring of remote cardiac implantable devices (ICD)?

a) No

b) Yes

10. Do you use an app or other type of plataform (not included remote monitoring of ICD) to control your patients?

a) No

b) Yes, please write which one…….

11. What type of patients are included?

a) Heart failure patient

b) LVAD patient, whether enlisted or not for heart transplant

c) Heart transplant patient

Design requirements for Patient Edge Gateway

12. Would you be willing to skip in-person visits with a telephone call or video chat?

1 (totally disagree)	2	3	4	5 (totally agree)

12. Would you find interesting the possibility to up titrate heart failure medications with a protocol through the platform?

1 (totally disagree)	2	3	4	5 (totally agree)

13. What functionalities would you consider useful for the patient to have on this device?

grade them from 1 (less useful) to 5 (more useful)]

	1	2	3	4	5
Chat with other patients					
Chat with a clinician					
Videochat with a clinician					
Medication reminders					
Medical visits reminders					
Statistics to track weight, blood pressure and heart rate records.					
Alerts to the doctor in case of altered parameters					

Educational material (nutrition, physical exercise…)					
Measurement of sleep: deep and light sleep phases, sleep interruptions.					
Measurement of daily activity: steps, distance, calories, floors climbed					
INR in anticoagulated patients					

Design requirements for Clinical Site Backend

14. What parameters would you consider useful to monitoring heart failure patients with an app? [grade them from 1 (less useful) to 5 (more useful)]

	1	2	3	4	5
Weight, weight body fat, skeletal muscle and body water					
Blood pressure– excluding patients with VAD					
Heart Rate (continuous assessment by intelligent watch)					
3 lead ECG evaluation.					
Peripheral capillary oxygen saturation					
Sleep: deep and light sleep phases, sleep interruptions.					
Steps, distance, calories, floors climbed					
Fluid balance (intake/diuresis)					
Sleep quality					
Adherence to prescribed medication					
Nutrition intake					
Circadian rhythm and activity log					
Patient living environment data					

15. Do you like all clinical data (medical history, laboratory tests, echocardiography, echocardiography, device interrogation) to be available on the platform?

1 (totally disagree)	2	3	4	5 (totally agree)

16. Would you like to receive warnings about patient health status?

1 (totally disagree)	2	3	4	5 (totally agree)

17. Which warning would you consider more useful? (grade them from 1 to 5)

	1	2	3	4	5
Atrial fibrillation/flutter (if previous sinus rhythm)					
High heart rate					
Rapid weight increase					
Desaturation					
High blood pressure (>180/110)					
Activity decrease					
Change in symptoms					

18. What do you think is the best way to receive notifications?

a) E-mail
b) Mobile message
c) App notification
d) Only when entering the platform

19. Which way do you prefer to consult patient data?

a) Mobile app
b) Computer program
c) Web

20. Would you like to receive suggestions about patient management generated by artificial intelligence?

1 (totally disagree)	2	3	4	5 (totally agree)

21. How often would you be willing to consult your patients' data?

a) Daily
b) Once a week
c) Once a month
d) Only when in scheduled visits
e) Only when receiving alerts

Retention in the clinical setting

22. How useful do you consider a platform like RETENTION (see page 1) for your Clinical practice?

1 (not useful)	2	3	4	5 (extremely useful)

23. What do you think is the main limitation to introduce a system like RETENTION in clinical practice?

a) Economic cost
b) Doctors lack of interest
c) Privacy problems

d) Patients lack of interest

e) Doctors lack of time

f) Other. Specify____

24. Which barriers do you consider more determinant to the correct use of RETENTION solution? (Grade them from 1-no determinant- to 5 – very determinant).

	1	2	3	4	5
Patients difficult with new technologies					
Doctors lack of time					
Doctors' perception of usefulness					
Administrative barriers					
Patient access to mobile phone/tablet					
Patients lack interest					
Patients' perception of usefulness					

25. Which ethical considerations do you think is more relevant? (Grade them from 1-non important-to 5 – very important).

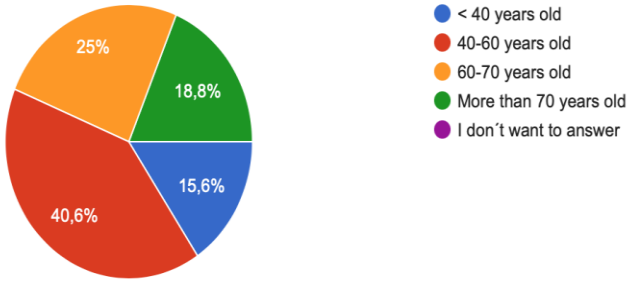
	1	2	3	4	5
System safety to informatics attacks					
Use of data by others					
Share hospital data with an external system					
Responsibility about altered parameters reported					
Responsibility about telematics clinical actuations					

Appendix 9.2: Questionnaires and Interview answers

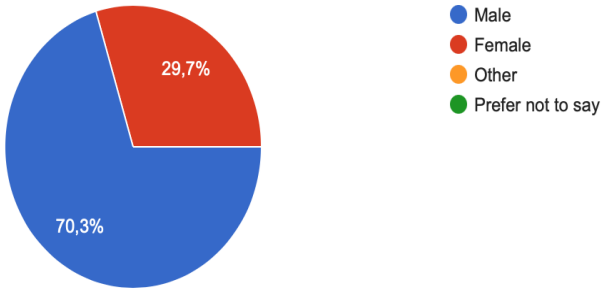
Patients` answers

Please select your age group:

64 respuestas

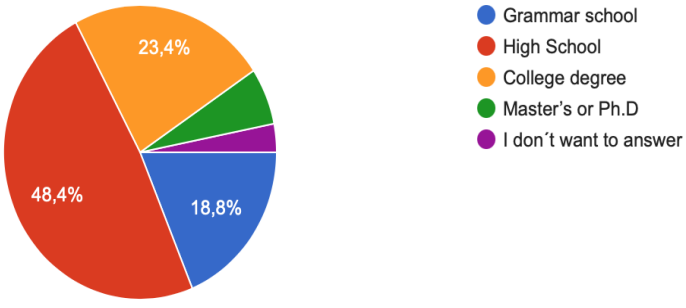


Please select your sex:

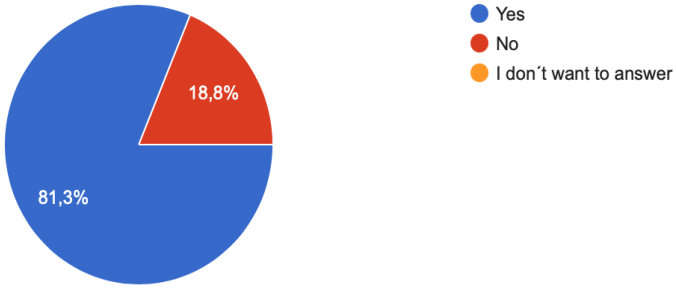


What is your education level?

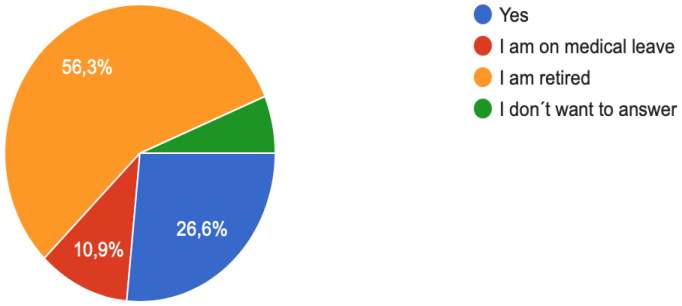
64 respuestas



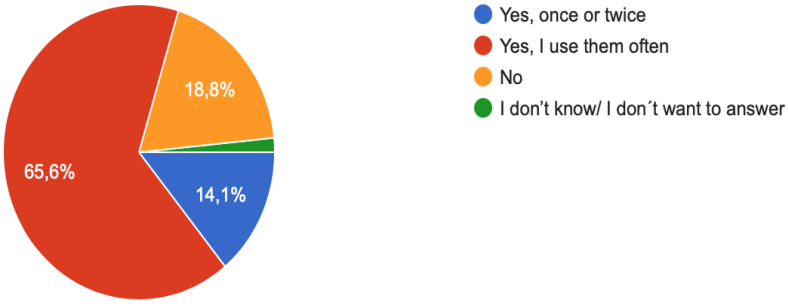
Have you ever used a personal computer (PC)?



Are you currently working?



Have you ever used a digital health device? (Measuring Heart rate, blood pressure, oxygen saturation, etc)



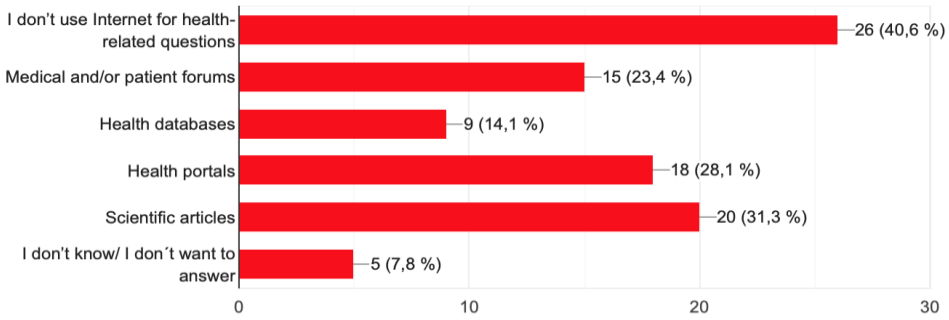
What type of mobile phone do you have?

64 respuestas

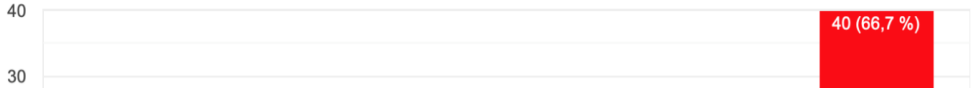
How would you rate your e-skills?

When you search the internet about your health, what type of web sites do you look for? (You can select more than one)

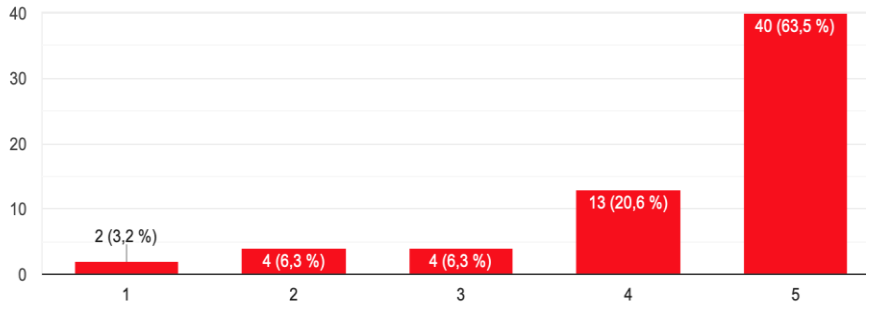
64 respuestas



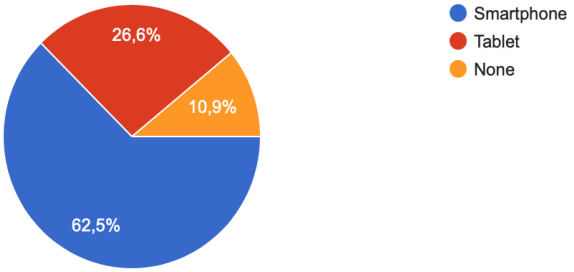
If your doctor recommends it, would you use a mobile app or web application to control your health status?



Would you be willing to wear a device (such as a wristwatch) that would monitor some of your health parameters, such as pulse, daily activity, etc.?

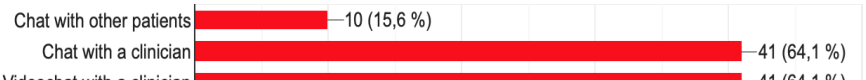


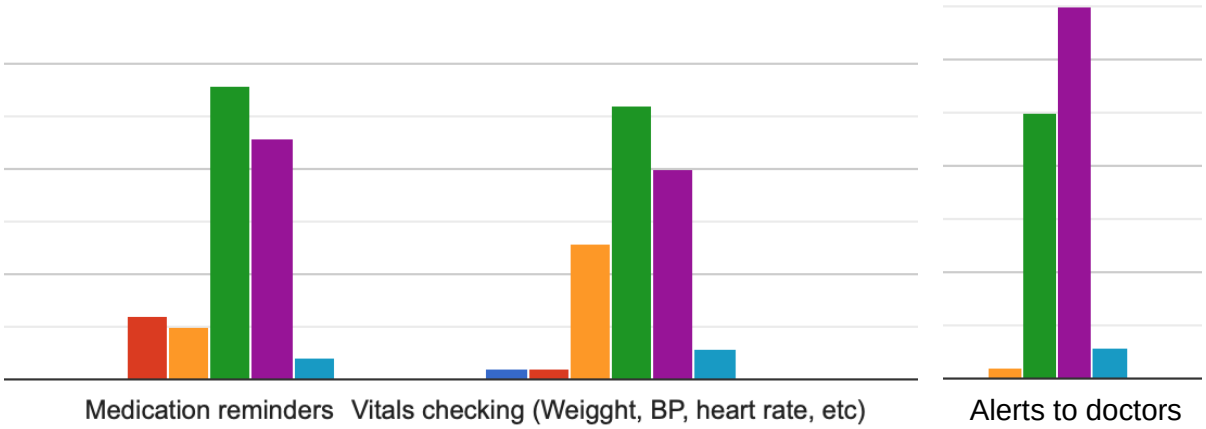
If we grant you a screen device to introduce some of your health information, which do you prefer?

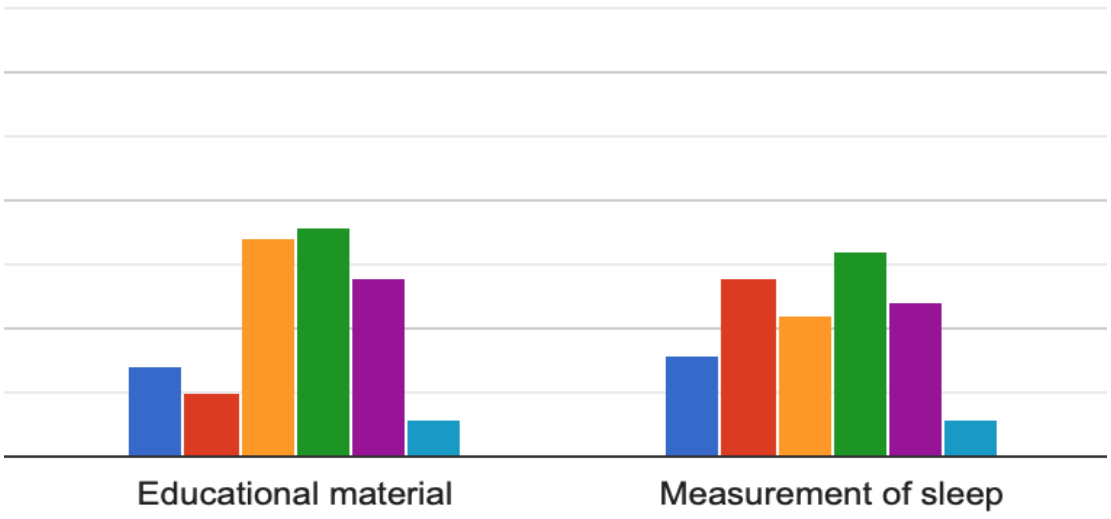


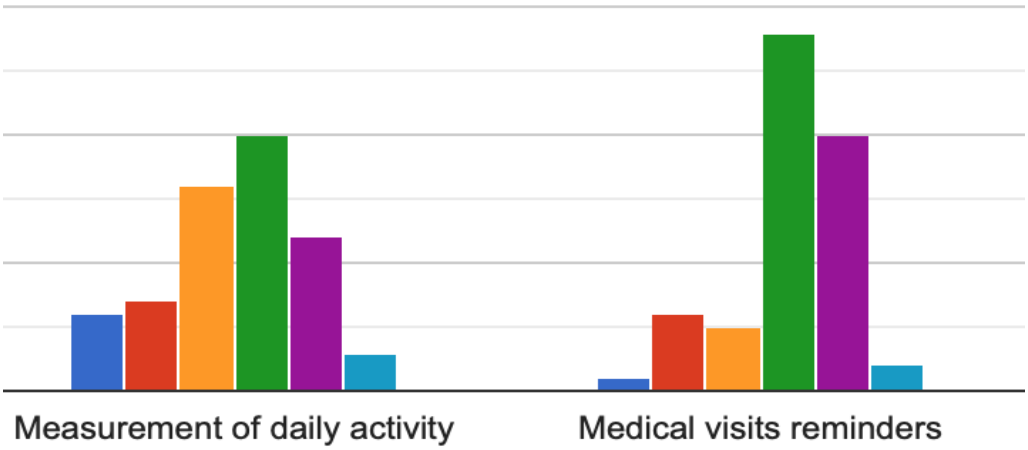
What functionalities would you like to have on this device? (Please select as many as you wish)

64 respuestas

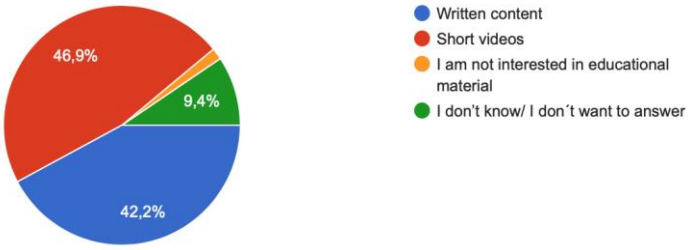



Medication reminders
Vitals checking (Weigght, BP, heart rate, etc)
Alerts to doctors

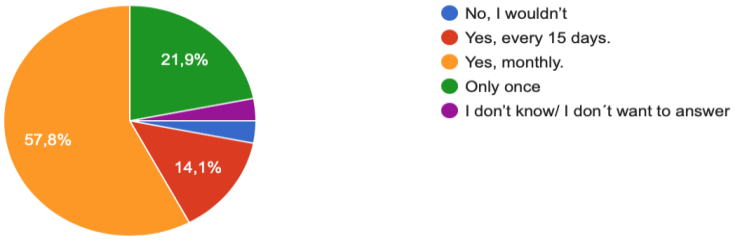

Educational material
Measurement of sleep



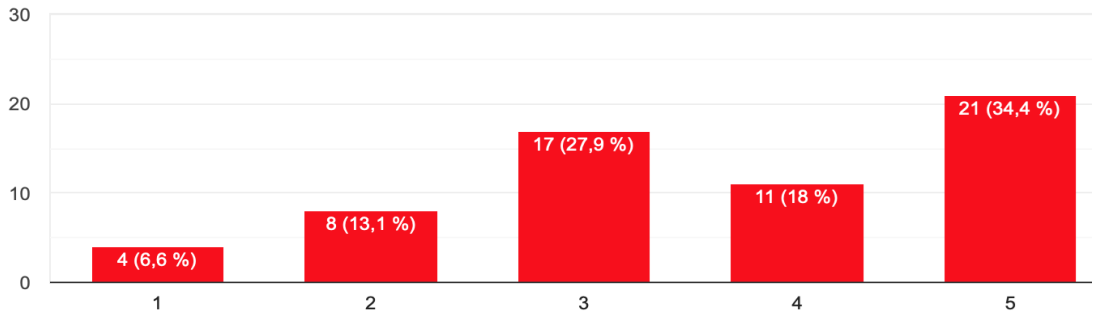
If the platform has educational content about nutrition, physical exercise, prevention of heart failure decompensations, etc., which format would you prefer?



Would you be willing to perform a 15-minute questionnaire on symptoms or quality of life? If so, on what basis?

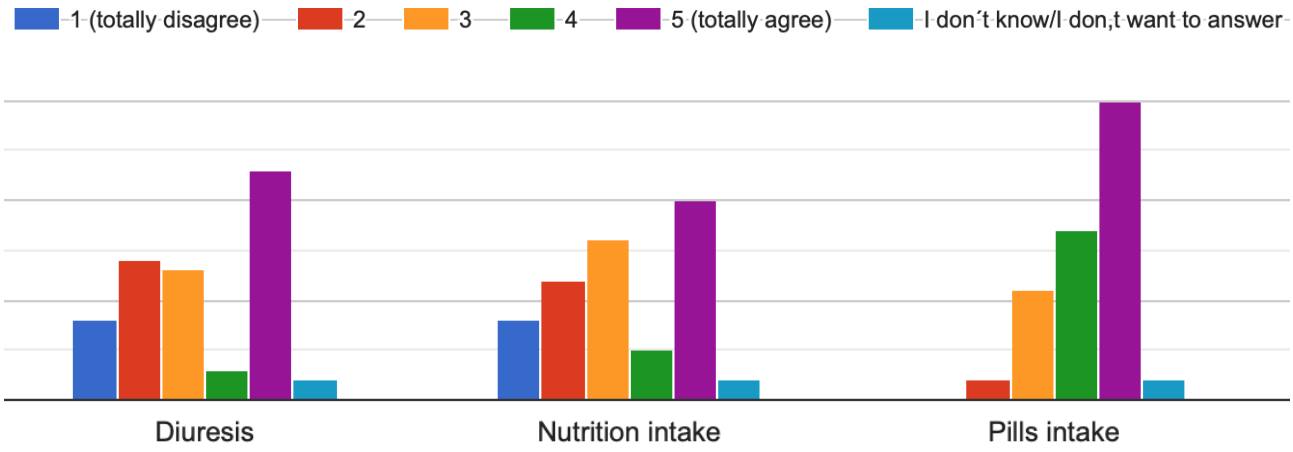


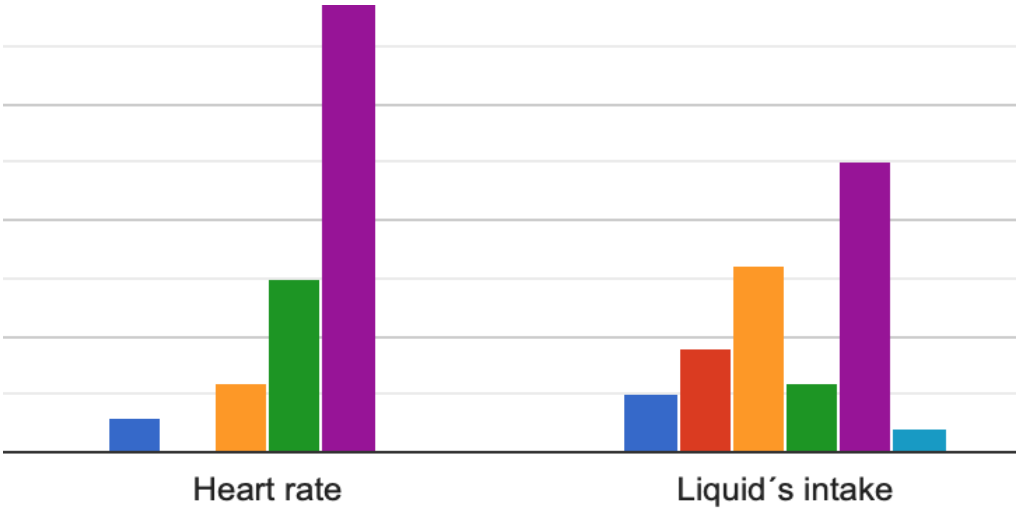
How much would you agree to have a plug-in device at home that would collect information on sunlight, humidity, and pollution?



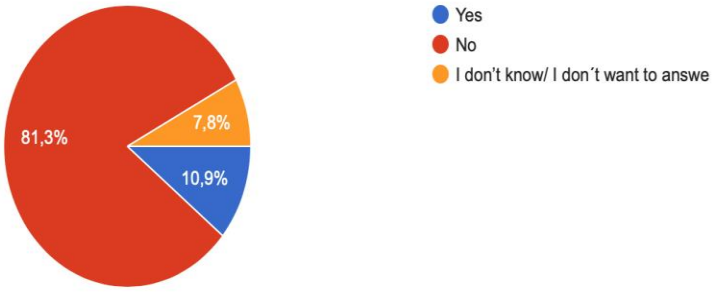
How much time per day would you be willing to spend on a platform (or mobile app) to monitor your health?

Which of the following measurements would you be willing to perform daily?

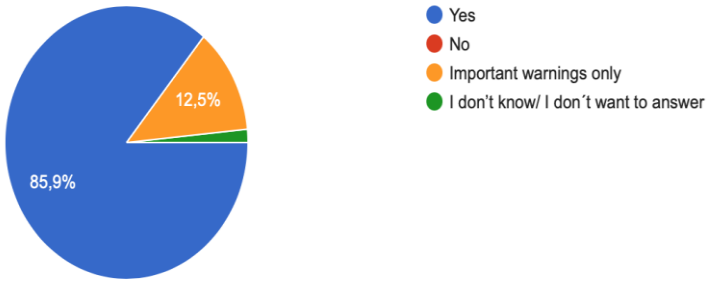




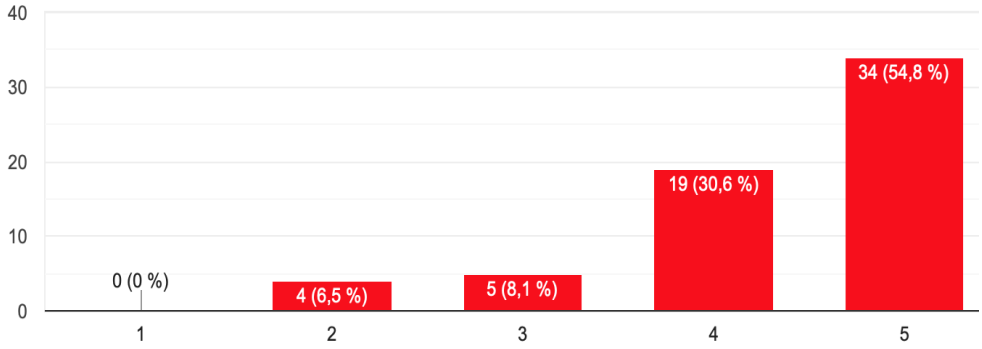
Would you prefer to maintain (store) some of the information in the platform private, non-availablefor your doctor?



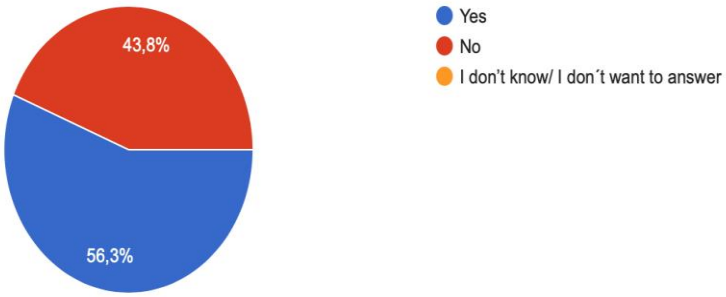
Would you like to receive warnings and recommendations from your doctor if altered parameters are detected?



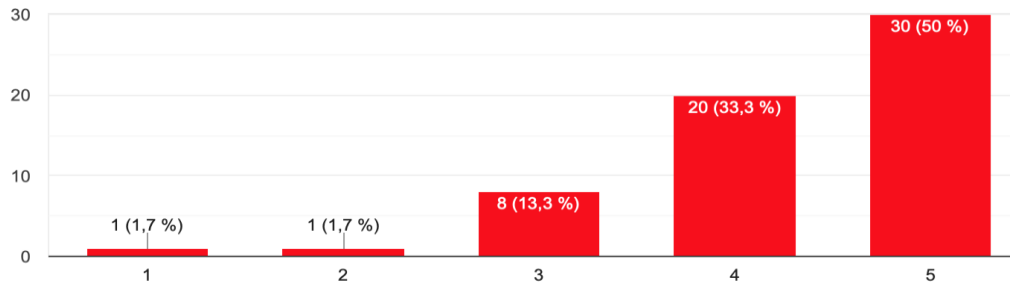
How much would you agree to give consent to this virtual platform to connect to your medical records at the hospital, so that we could more easily obtain information on your laboratory tests results, outpatient visits, etc.?



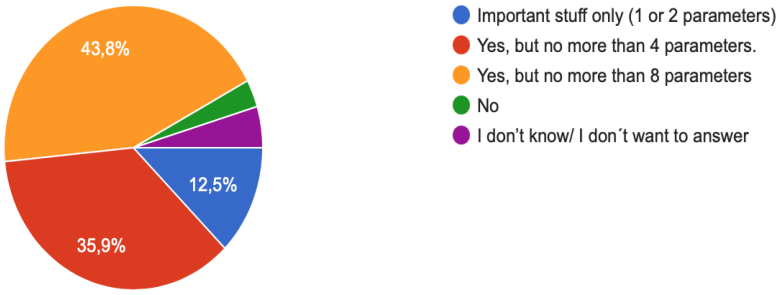
Would you need your caregiver/companion to help you with the platform (or mobile app)?



How much would you like your caregiver/companion to have an active role (filling questionnaires, having access to educational material, medical visits reminders, etc) in the platform?

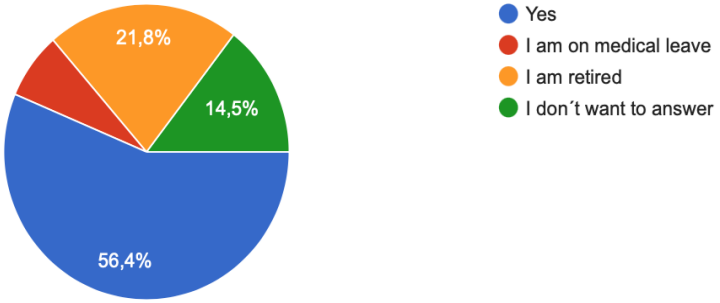


if need be, would you be willing to manually insert information to the platform (or application) on the device or the internet?

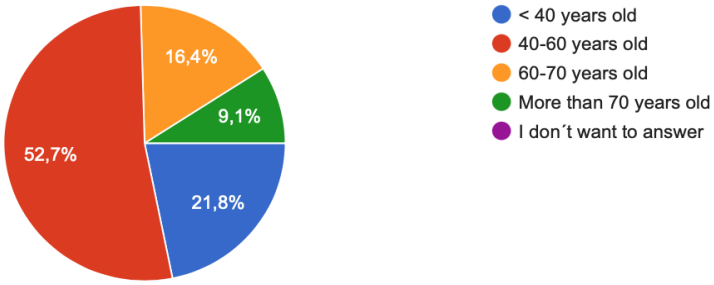


Caregivers´ answers

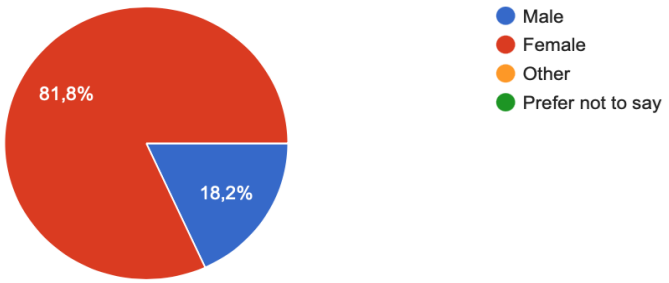
Are you currently working?



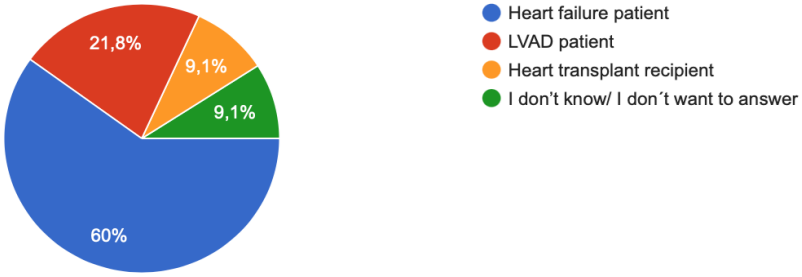
Please select your age group:



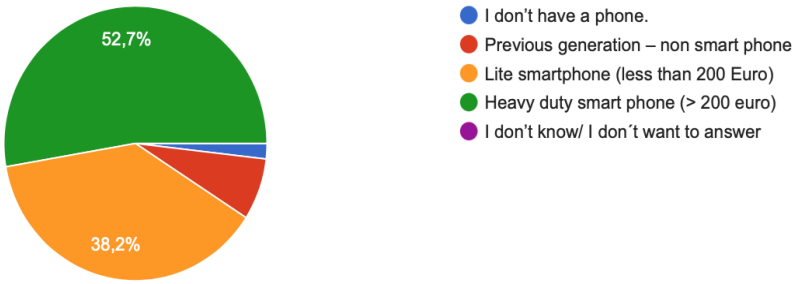
Please select your sex:



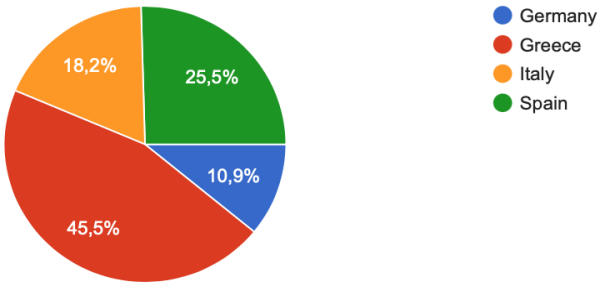
Please select which of the following best represents the person you care of



What type of mobile phone do you have?

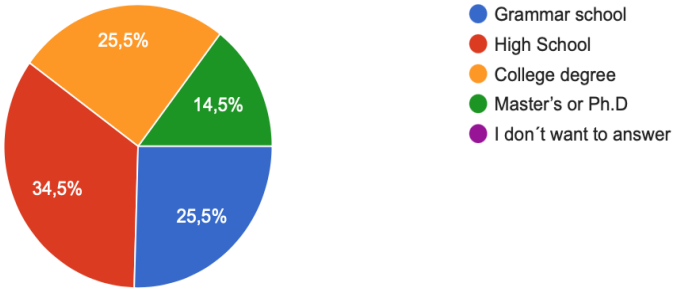


Please, select your country

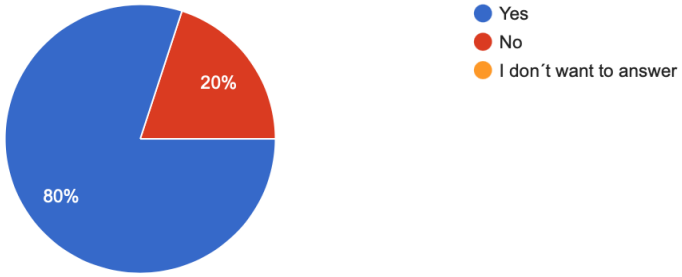


Select your internet connection at home:

What is your education level?

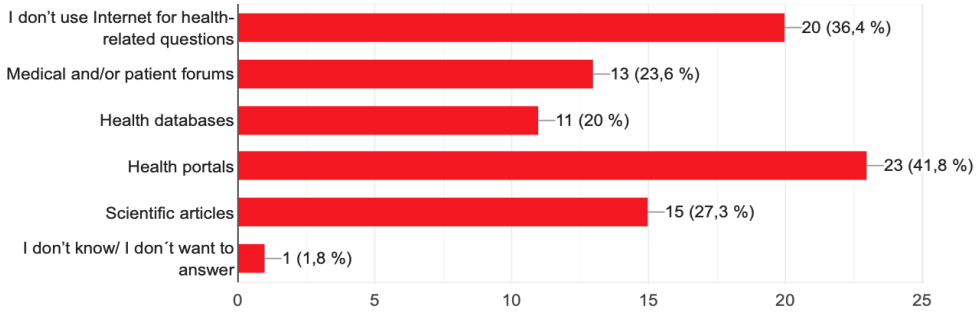


Have you ever used a personal computer (PC)?

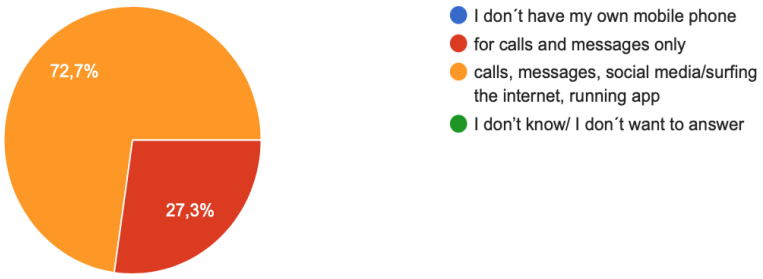


How would you rate your e-skills?

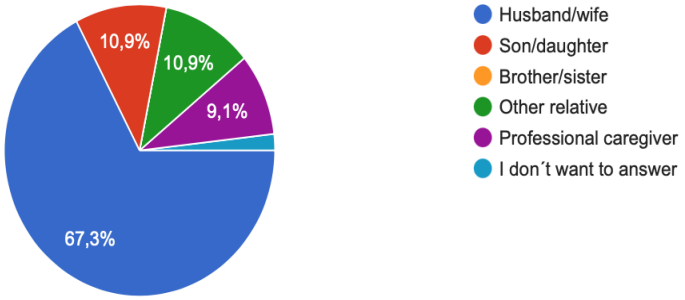
When you search the internet about your health, what type of web sites do you look for? (You can select more than one)



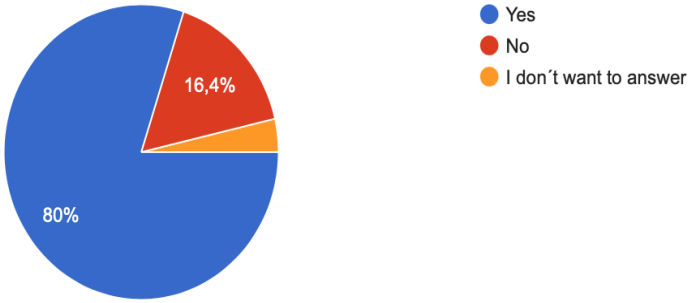
What do you use your mobile phone for?



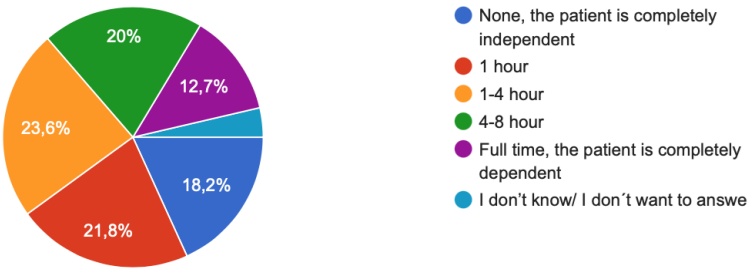
Describe your relationship with the patient



Are you the main carer?

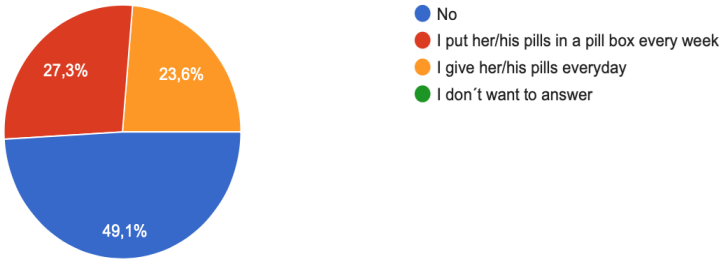


How much time per day do you spend on patient care?

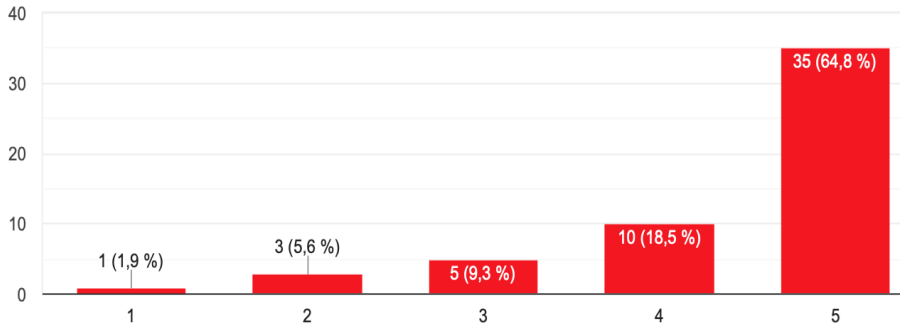


Do you assist the patient with medication adherence?

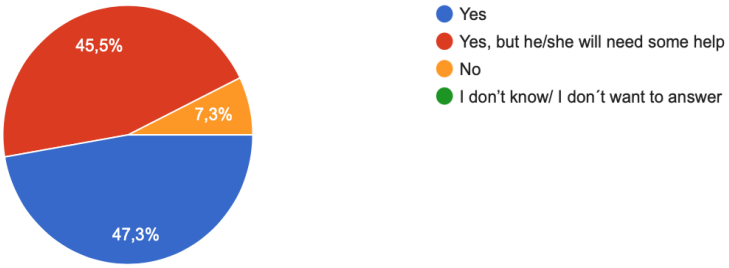
55 respuestas



If the doctor recommends it, would you be willing provide your own data to the mobile app

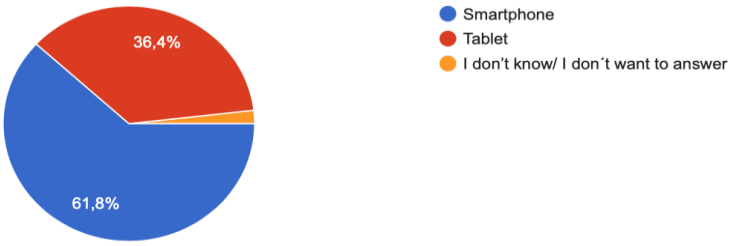


In your opinion, do you believe that the patient is able to use a smartphone/device to collect data related to his/ her health?

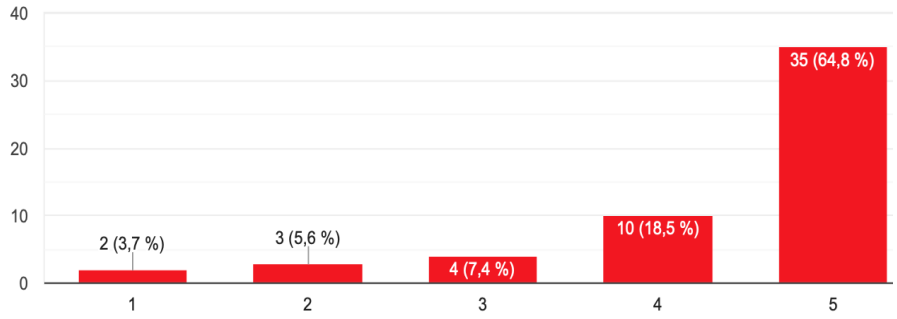


If we give you a screen device to introduce some of the patient's health information, which wouldyou prefer?

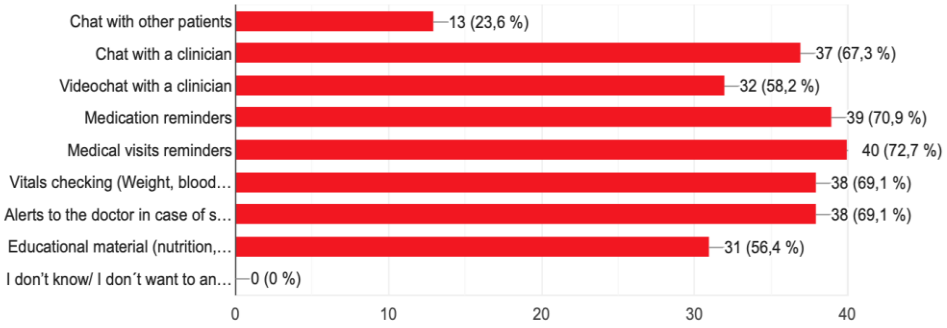
55 respuestas



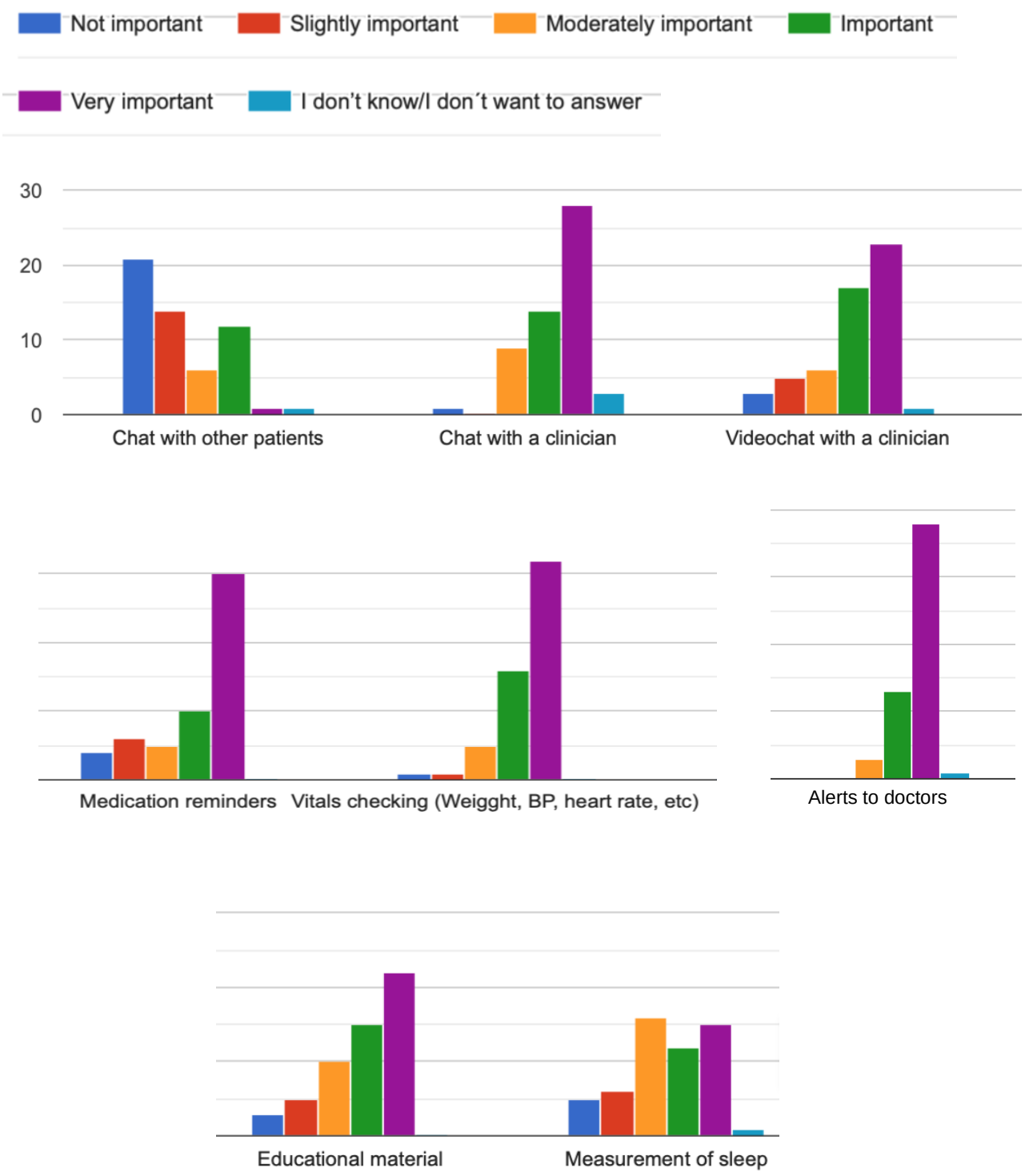
Would you be willing to help the patient to collect health data on a mobile app?

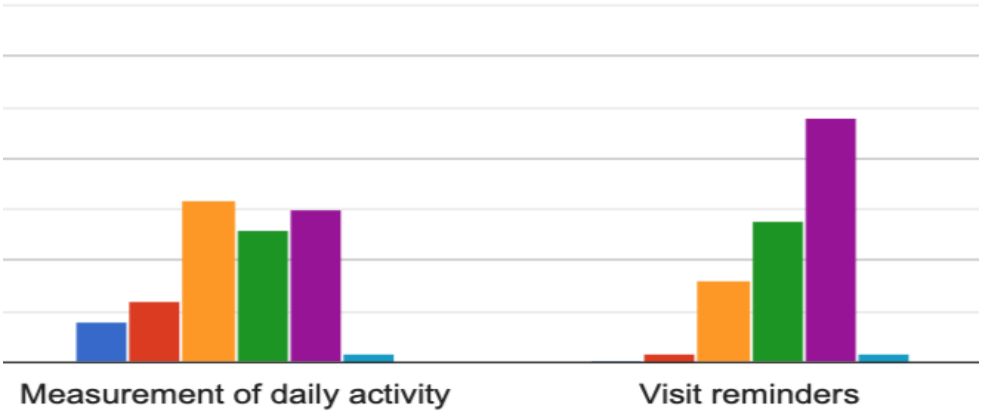


What functionalities would you like to have on this device? (Please select as many as you wish)

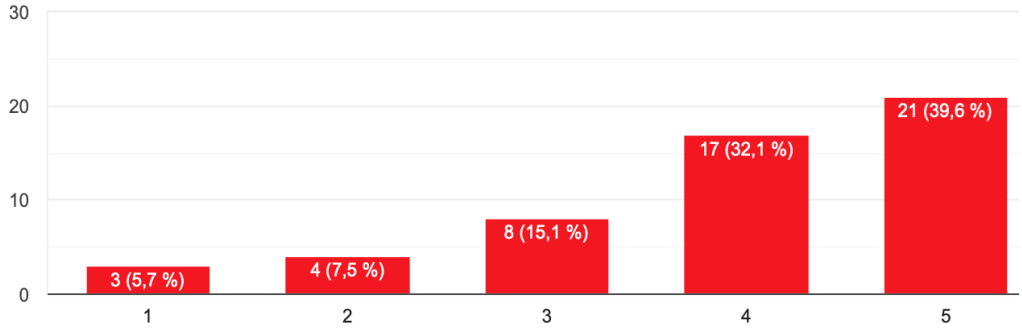


Could you rank the following device characteristics according to how important they are to you?

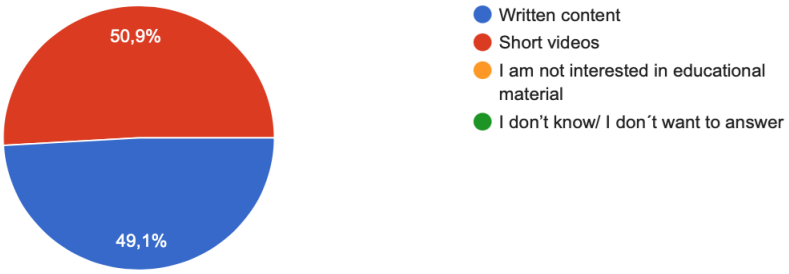




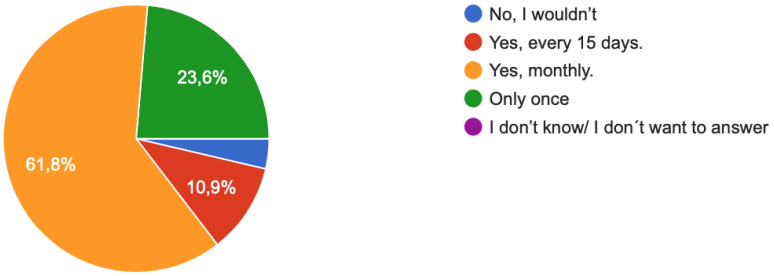
How much would you agree to have a plug-in device at home that would collect information on sunlight, humidity, and pollution?



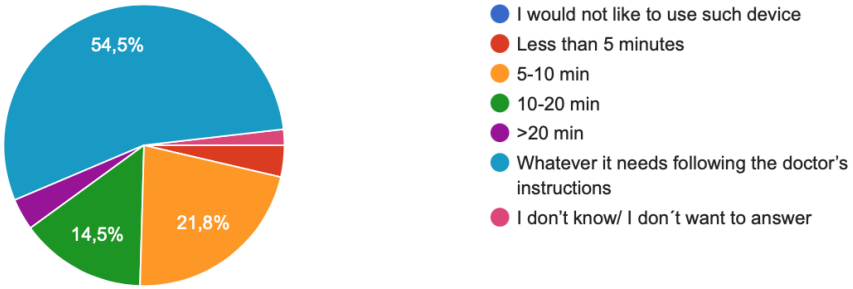
If the platform has educational content about nutrition, physical exercise, prevention of heart failure decompensations, etc., which format would you prefer?



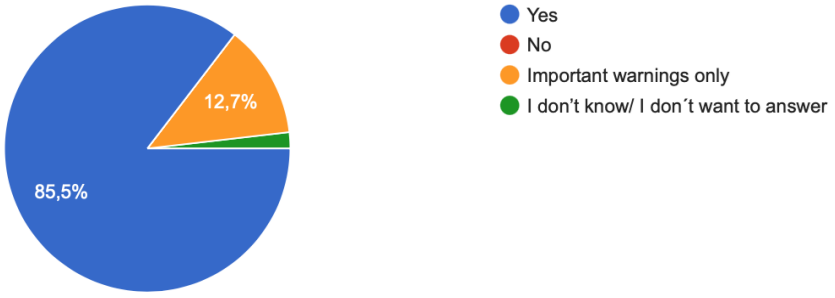
Would you be willing to perform a 15-minute questionnaire? If so, on what basis?



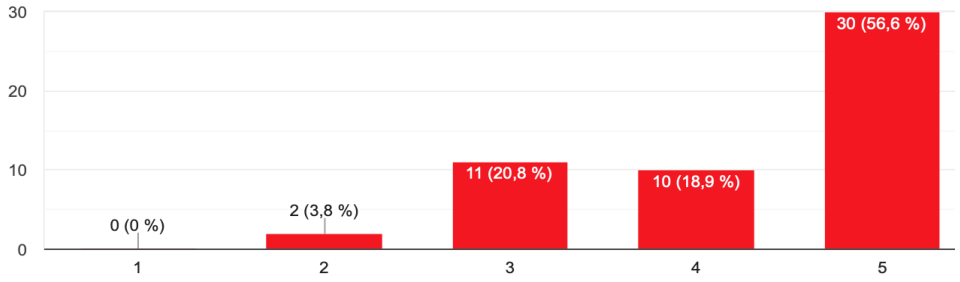
How much time per day would you be willing to spend on a platform (or mobile app) to monitor the patient´s health?



Would you like to receive warnings and recommendations from your doctor if altered parameters are detected?

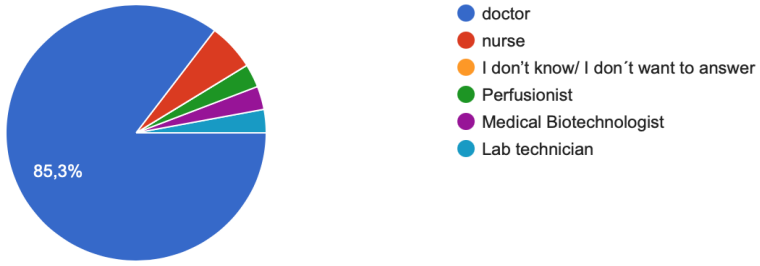


How much would you like to have an active role (filling questionnaires, having access to educationalmaterial, medical visits reminders, etc) in the platform?

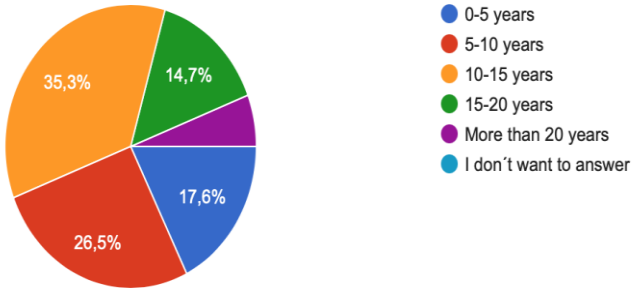


Clinicians´answers

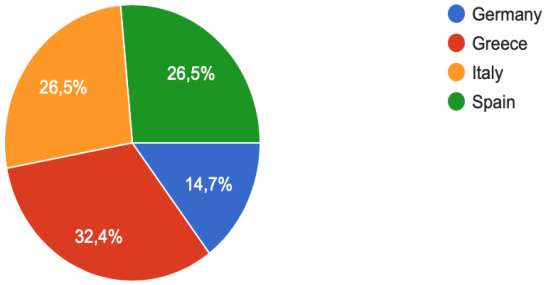
Select your background education



How long have you been practicing your profession?

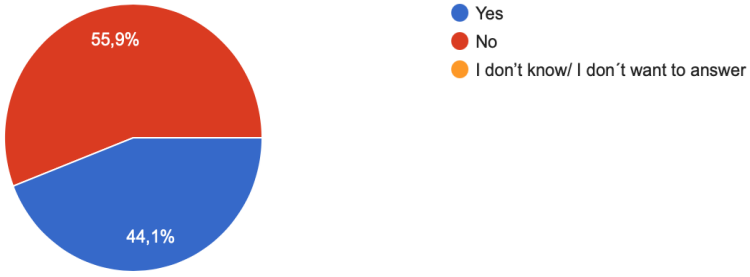


Please, select your country

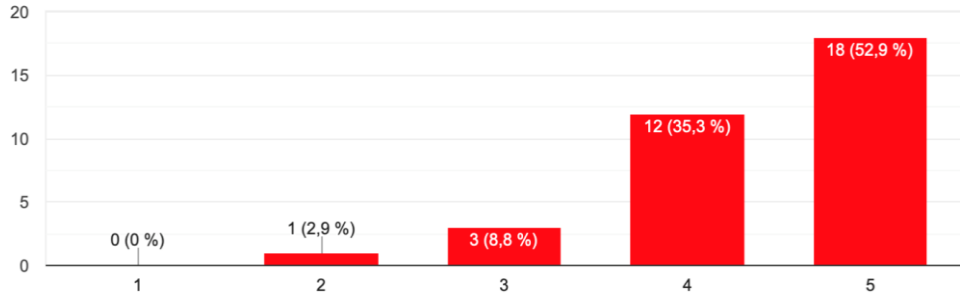


Have you got previous experiences with remote monitoring in heart failure patients?

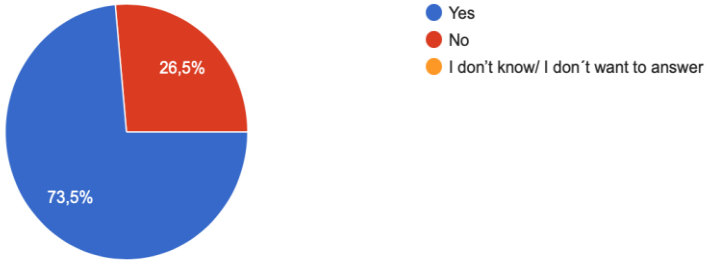
:



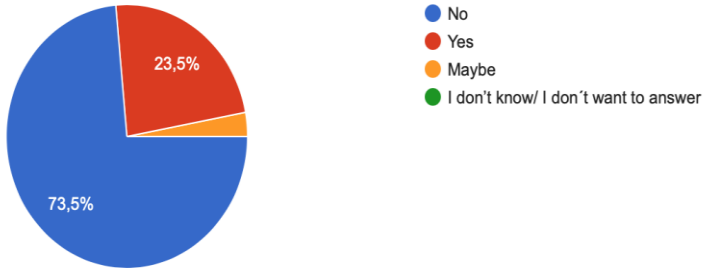
Do you think that a specifically designed app can improve the follow-up of patients with heart failure?



Do you/or someone from your team use remote monitoring of remote cardiac implantable devices(ICD)?



Do you use an app or other type of platform (not included remote monitoring of ICD) to control your patients?



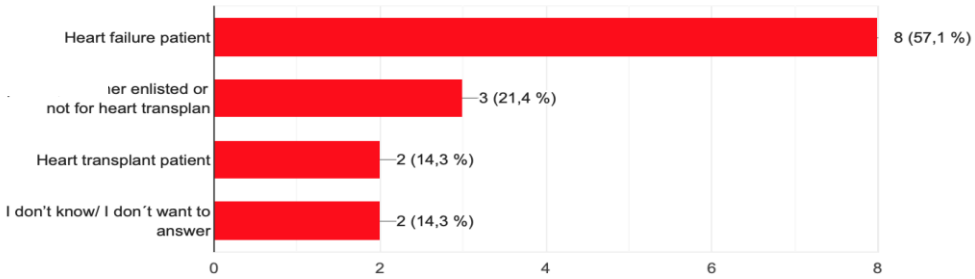
If you use an app or other type of platform (not included remote monitoring of ICD) to control your patients, please write which one

7 respuestas

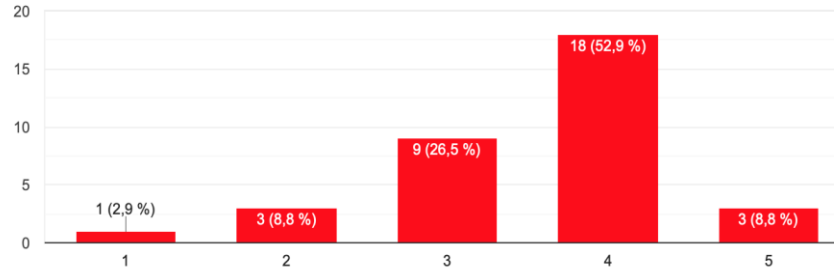
- m Heart
- MyPlan by Emma
- customized app
- Telemedicine HF program
- I participate in a clinical trial called HErmes-Trial, that allows you to monitor the weight, blood pressure, heart rate and daily control of symptoms trhough a mobile phone. In addition, it allows you to make video calls.
- Join Medical
- PA sensor

If you use an app or other type of platform to control your patients, what type of patients are included?

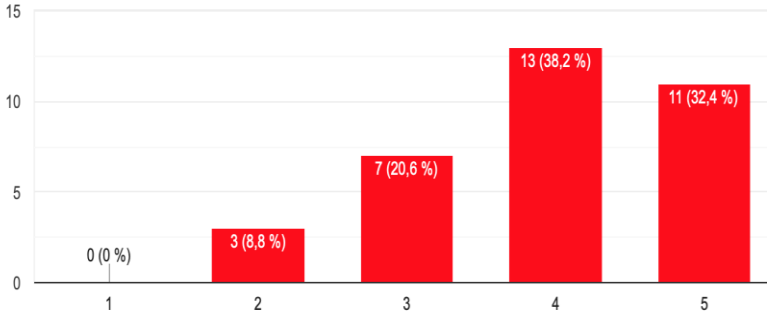
14 respuestas



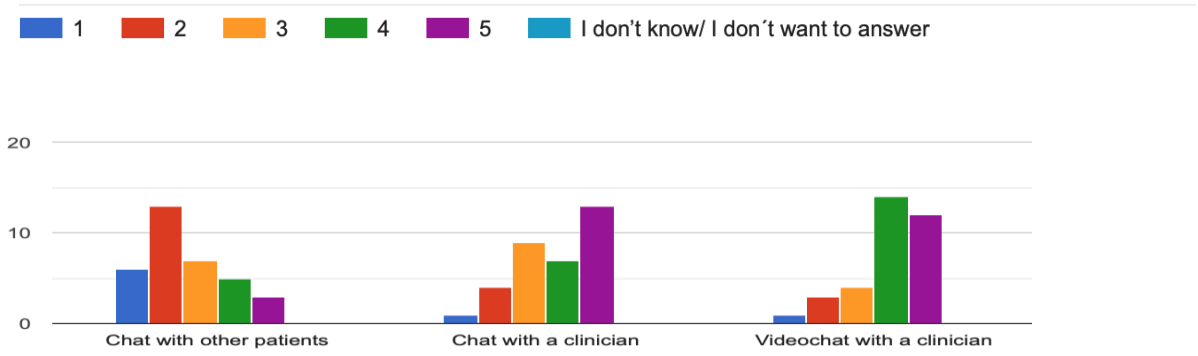
Would you be willing to skip in-person visits with a telephone call or video chat?

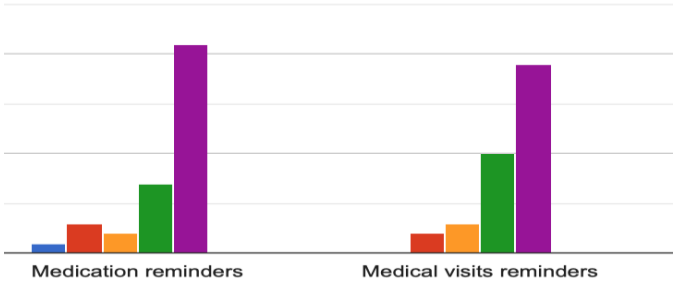


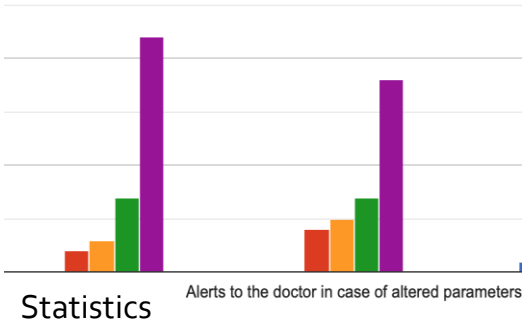
Would you find interesting the possibility to up titrate heart failure medications with a protocol through the platform?

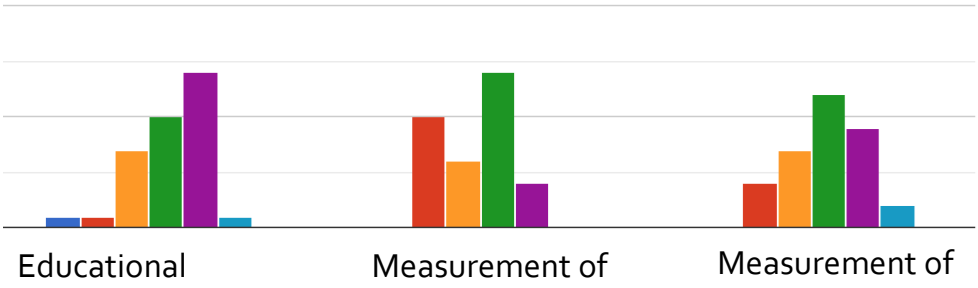


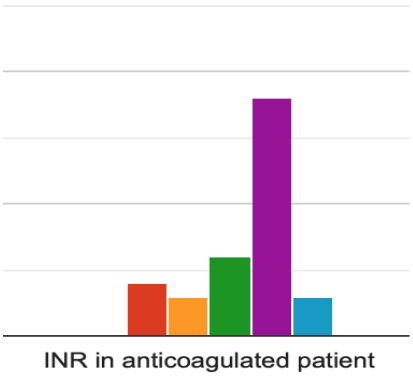
What functionalities would you consider useful for the patient to have on this device?Grade them from 1 (less useful) to 5 (more useful)]



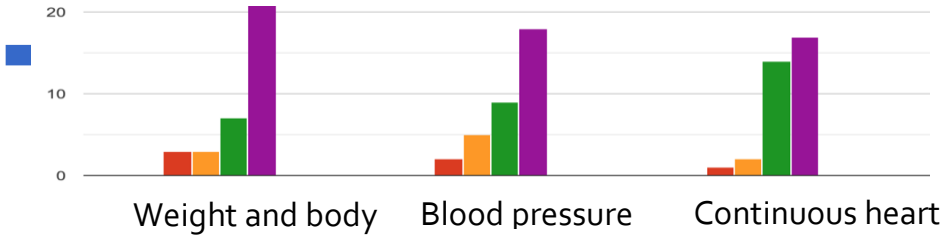

Medication reminders
Medical visits reminders

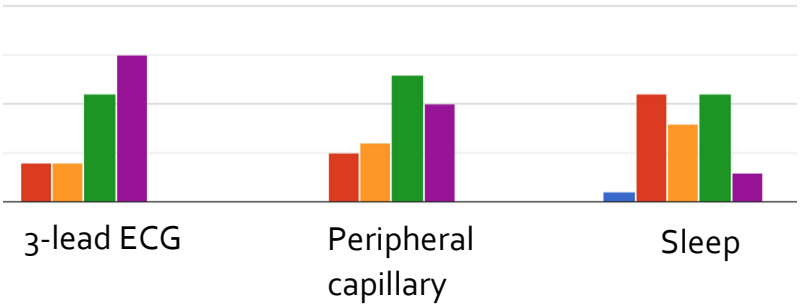

Statistics
Alerts to the doctor in case of altered parameters

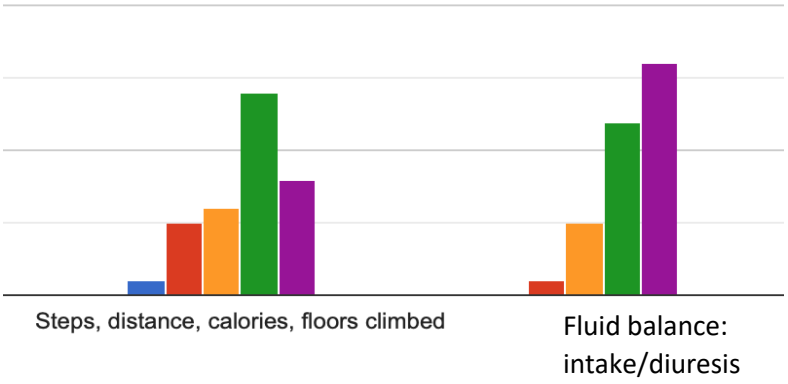

Educational
Measurement of
Measurement of

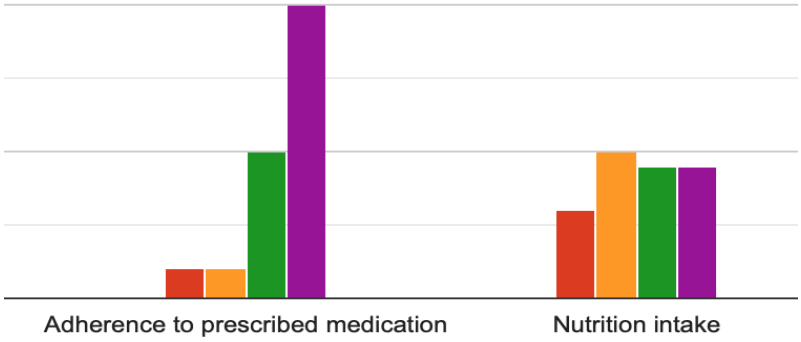

INR in anticoagulated patient

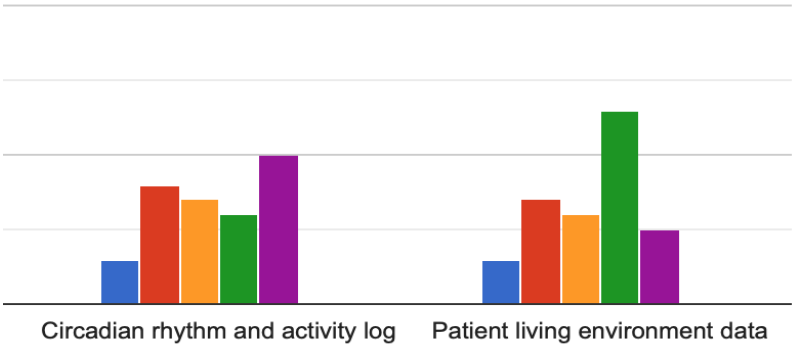
What parameters would you consider useful to monitoring heart failure patients with an app? [gradethem from 1 (less useful) to 5 (more useful)]



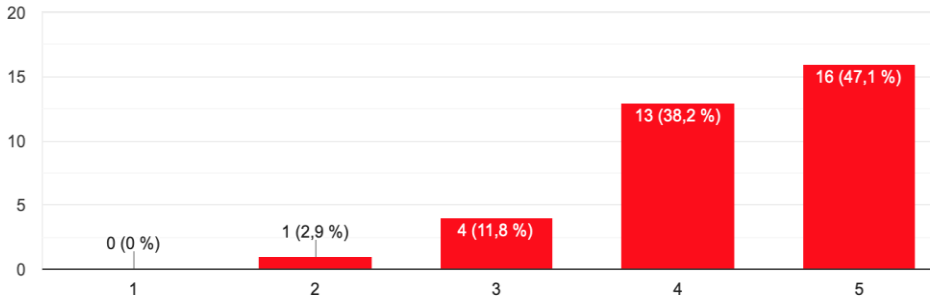




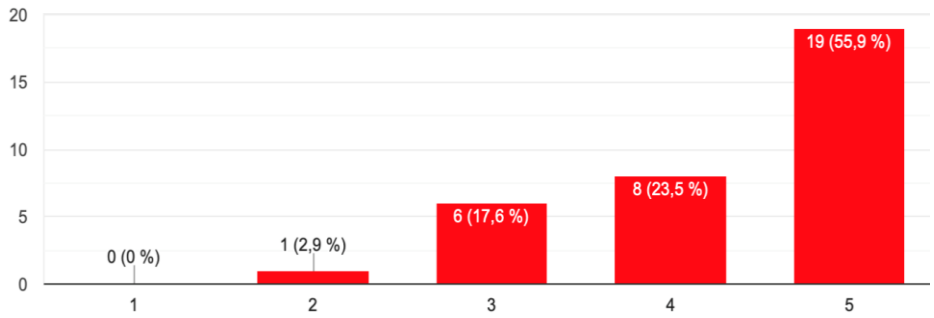




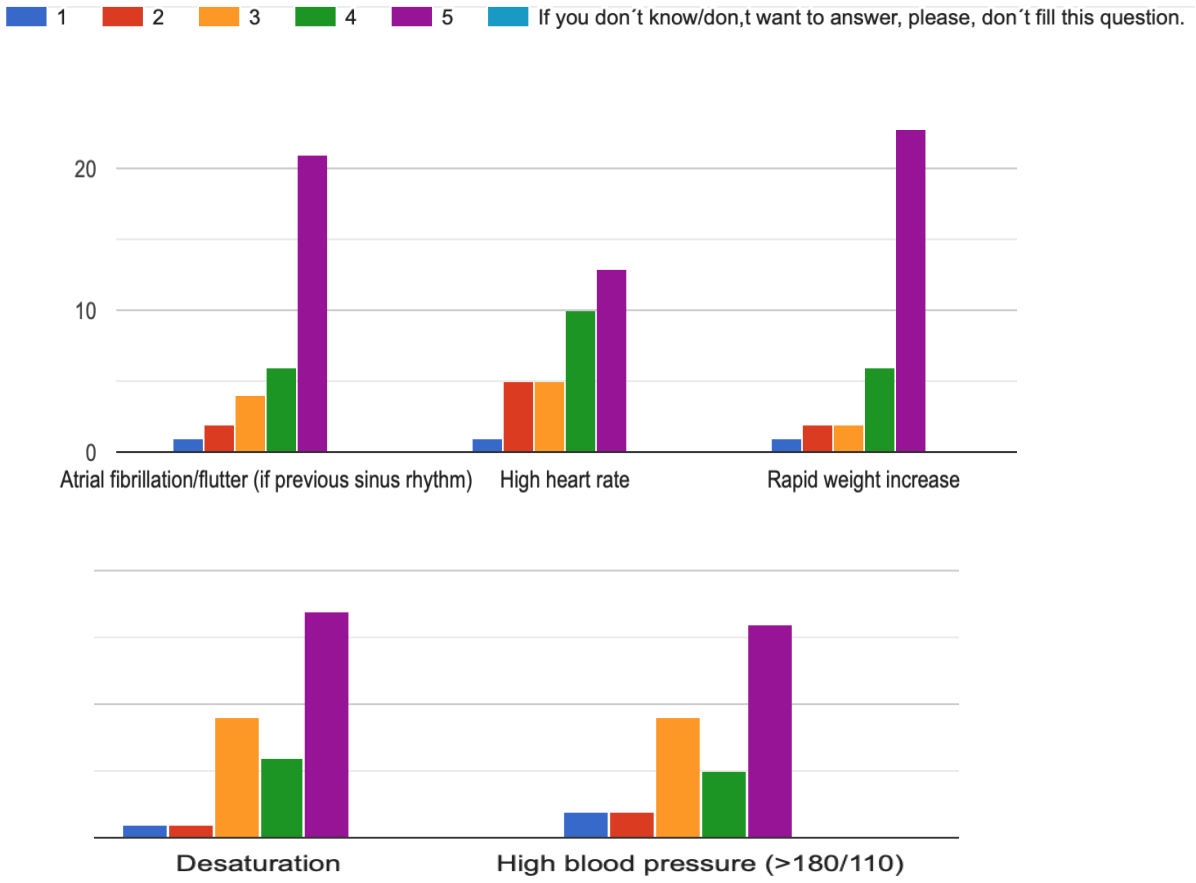
Do you like all clinical data (medical history, laboratory tests, echocardiography, echocardiography, device interrogation) to be available on the platform?

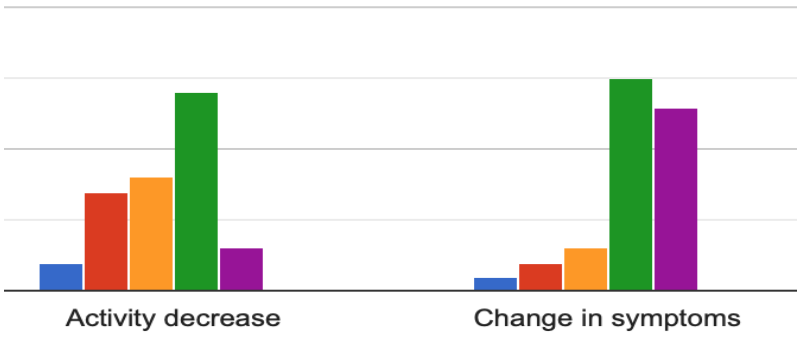


Would you like to receive warnings about patient health status?

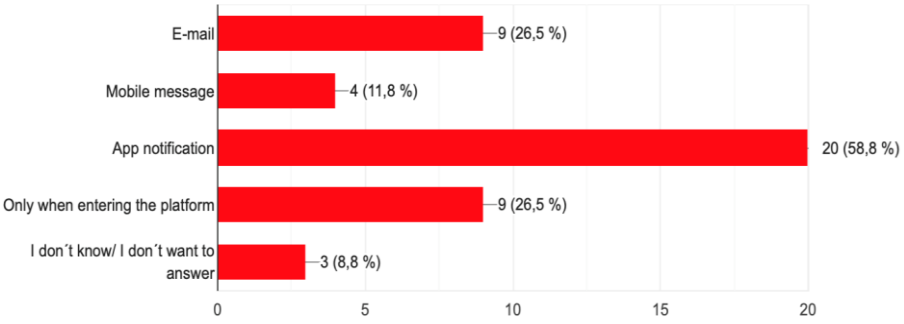


Which warning would you consider more useful? (Grade them from 1 to 5)

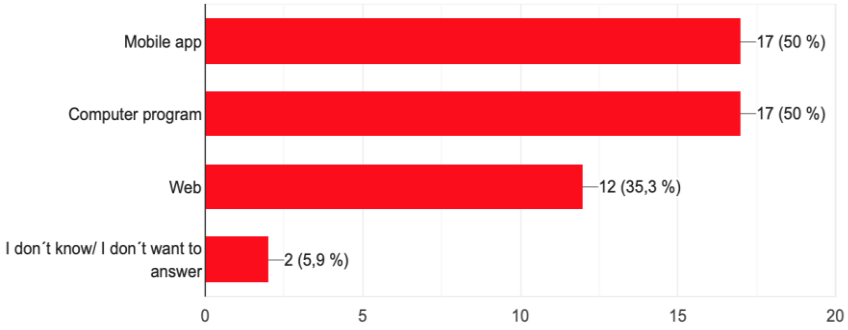




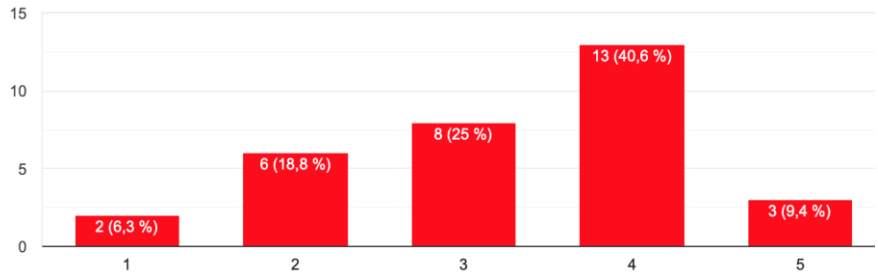
What do you think is the best way to receive notifications?



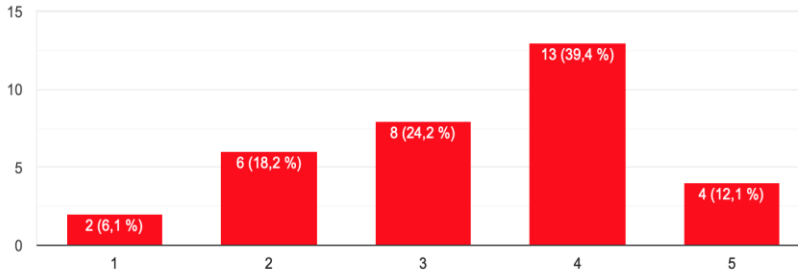
Which way do you prefer to consult patient data?



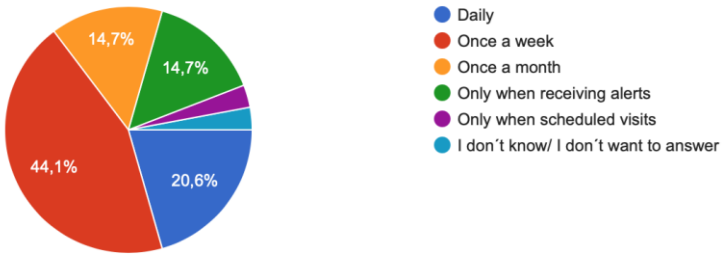
Would you like to receive suggestions about patient management generated by artificial intelligence?



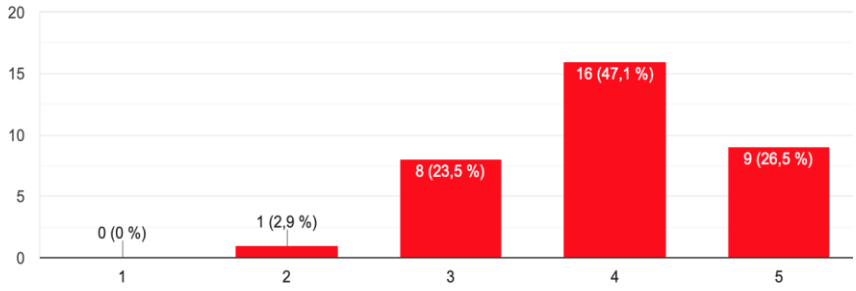
Would you like to receive suggestions about heart failure treatment titration automatically generated?



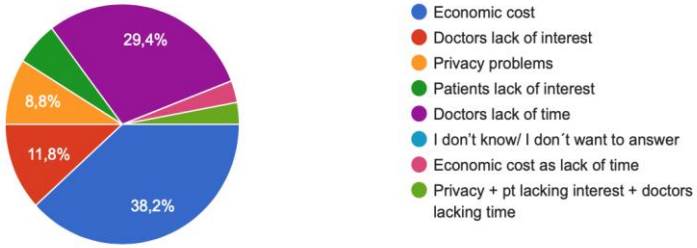
How often would you be willing to consult your patients' data?



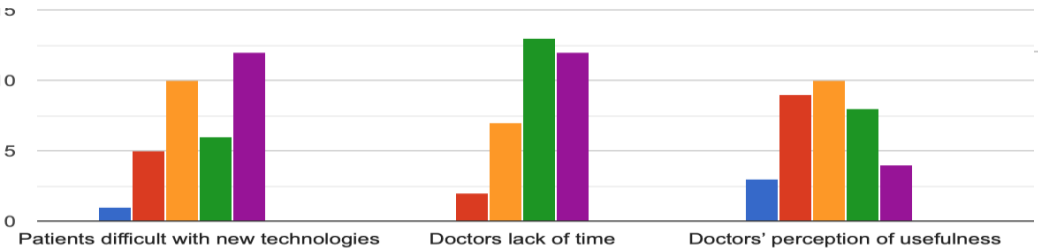
How useful do you consider a platform like RETENTION (see description in the introduction) for your Clinical practice?

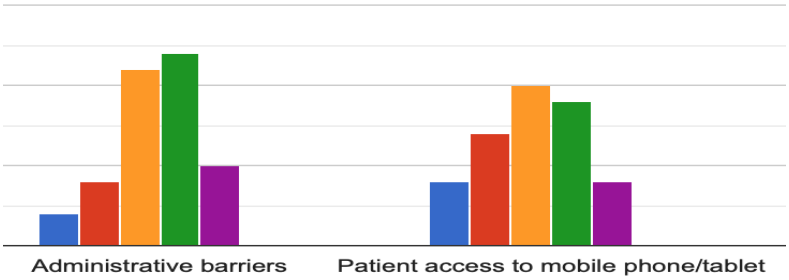


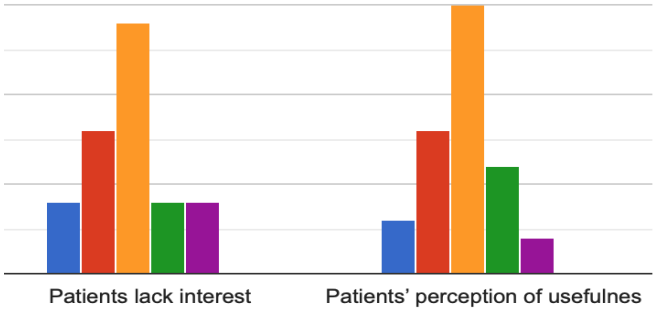
What do you think is the main limitation to introduce a system like RETENTION in clinical practice?



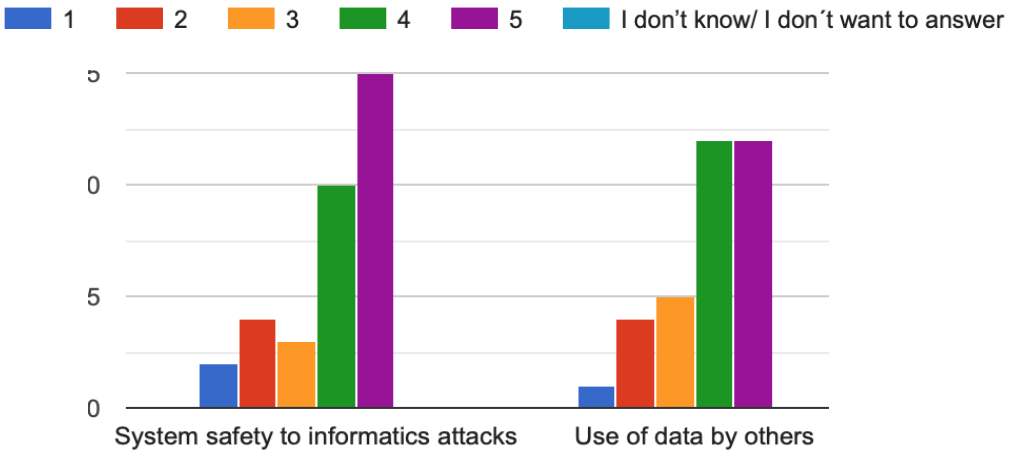
Which barriers do you consider more determinant to the correct use of RETENTION solution? (Gradethem from 1-no determinant- to 5 – very determinant)

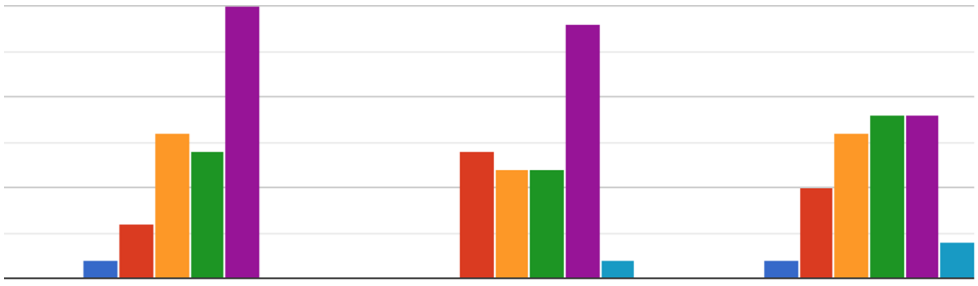






Which ethical considerations do you think is more relevant? (Grade them from 1-non important-to 5–very important).





Sharing hospital data with an external system

Responsibility about altered parameters

Responsibility about telematic clinical actuations

Interview with Mr. Michael Papadakis (OCSC IT Manager)

Technical Requirements

- Is there availability of a complete and accurate Electronic Patient Record (EPR) and appropriate Information Systems to accommodate and support it (HIS, LIS, RIS/PACS)? If not, what is missing?

Yes. In OCSC we maintain a complete EPR for more than 20 years, containing detailed records of the patient exams and results, doctor's letters, diagnosis, medical procedures, outpatient clinic visits, medical imaging, and costing.

- Is there complete and accurate historical data in adequate depth of time? Please specify.

Yes. Our medical records extend to more than 20 years for all afore mentioned data.

- Can the RETENTION system be connected to the HIS/ERP or other hospital system?

If the appropriate connectors (interfaces, APIs, etc.) are provided, yes. All our Information Systems are HL7 and DICOM compliant and ad-hoc custom-made interfaces (on-line of off-line/batch) can be developed.

- Is there a compliance with EPR standards (e.g., HL7, DICOM, etc.), so that data can be interchanged between medical facilities, hospitals, etc.? If not, what does it exist?

Our Information Systems (HIS, LIS, CIS, RIS, etc.) are fully HL7 and DICOM 3.0 compliant.

- Do you agree reaching an agreement on the exact technical specs (both functional and non-functional) of the platform from the various user groups and project stakeholders, e.g., clinical doctors, lab doctors, consultants, nurses, technical personnel, etc.? If yes, how? if not, why?

Yes. We can reach an agreement with our users. I propose a complete questionnaire for the beginning to note the various requirements and preferences, and then a series of 2-3 on-line meeting to discuss the detains (technical and non-technical).

Barriers

- Reluctance or ignorance of the high management to support the project (with appropriate human resources and availability or working time)? Why?

The high management of OCSC is fully informed of the details and benefits of the project, as well as the scope of work, and they are fully support the whole effort.

- Reluctance of medical staff (doctors) to get involved in the project due to the lack of time (especially in the times of the pandemic) or not (please specify)?

All four OCSC doctors involved in the project are selected after their brief and are fully informed for the work for the project. They all agree to work for it and are fully committed to the project. Because of their involvement with Heart Failure patients, they also have great scientific interest in the project.

- Is there a lack of experienced technical personnel for both: (1) development & use of modern software tools (2) data processing skills combined with appropriate clinical knowledge (database management and data retrieval, data evaluation and cleansing, application of appropriate algorithms, evaluation of results, educated feedback and interpretation of results), or not (please specify)?

OCSC IT Dept. has available 2 very experienced computer engineers for the use of modern data-processing tools, and database administration and management. They also have more than 20 years' experience in advanced data processing and transforming raw data into information used both for medical and

managerial purposes. For the time being, there is no programmer in OCSC to develop any software, but this lack is expected to be covered within the following months.

- In some cases, additional data are required from the patients, and the follow up of them is not so regular, so is it sometimes difficult to get in touch with them? How do you suggest solving it?

All OCSC patients of the Heart Failure Unit are connected to OCSC and are closely monitored by the Unit personnel. If any additional data are needed, they can be collected through additional visits of the patients to the outpatient clinic of OCSC, of though telephone interviews from our liaison nurses.

- Do you estimate any cost for the above?

Cost estimation would be difficult for the time being. When specific need arises, a more accurate cost estimation can be made. In general, I don't think the costs would be a severe issue, because most of the required infrastructure already exists in the framework of the normal hospital operation. Working costs, in most cases, can be covered within the project budget.

Interview with Mrs. Polychronopoulou (ATTIKON Hospital - NCUA - IT Manager)

Technical Requirements

- Is there availability of a complete and accurate Electronic Patient Record (EPR) and appropriate Information Systems to accommodate and support it (HIS, LIS, RIS/PACS)? If not, what is missing?
  Yes, there is availability.

- Is there complete and accurate historical data in adequate depth of time? Please specify.
  There is historical data from 2007.

- Can the RETENTION system be connected to the HIS/ERP or other hospital system?
  I suppose it can be connected using HL7 messages but there must be cooperation between software suppliers.

- Is there a compliance with EPR standards (e.g., HL7, DICOM, etc.), so that data can be interchanged between medical facilities, hospitals, etc.? If not, what does it exist?
  See the answer in question 3.

- Do you agree reaching an agreement on the exact technical specs (both functional and non-functional) of the platform from the various user groups and project stakeholders, e.g., clinical doctors, lab doctors, consultants, nurses, technical personnel, etc.? If yes, how? if not, why?
  We agree but there are no IT technicians available to support the project.

Barriers

- Reluctance or ignorance of the high management to support the project (with appropriate human resources and availability or working time)? Why?
  No, there is no reluctance or ignorance.

- Reluctance of medical staff (doctors) to get involved in the project due to the lack of time (especially in the times of the pandemic) or not (please specify)?
  No there is no reluctance.

- Is there a lack of experienced technical personnel for both: (1) development & use of modern software tools (2) data processing skills combined with appropriate clinical knowledge (database management and data retrieval, data evaluation and cleansing, application of appropriate algorithms, evaluation of results, educated feedback and interpretation of results), or not (please specify)?
  Limited experience for the time being.

- In some cases, additional data are required from the patients, and the follow up of them is not so regular, so is it sometimes difficult to get in touch with them? How do you suggest solving it?
  No, it is not difficult.

- Do you estimate any cost for the above?
  Not applicable.

Interview with Mr. Juan Manuel Martín Ginner (CIO, Hospital Puerta de Hierro-SERMAS)

Technical Requirements

- Is there availability of a complete and accurate Electronic Patient Record (EPR) and appropriate Information Systems to accommodate and support it (HIS, LIS, RIS/PACS)? If not, what is missing? Is there complete and accurate historical data in adequate depth of time? Please specify.

Yes, a complete EPR is available since year 2000 more or less containing all the hospital records of the patient: laboratory and imaging exams, medical reports, procedures

- Is there complete and accurate historical data in adequate depth of time? Please specify.

Missing Answer (see the above)

- Can the RETENTION system be connected to the HIS/ERP or other hospital system? Is there a compliance with EPR standards (e.g., HL7, DICOM, etc), so that data can be interchanged between medical facilities, hospitals, etc.? If not, what does it exist?

Yes, our Information Systems are HL7 and DICOM compliant. Our system is already connected with other systems (Horus: containing data from other SERMAS hospitals and facilities, MUP: electronic prescription system, SNS: national health system, system of alerts in Comunidad de Madrid…)

- Is there a compliance with EPR standards (e.g., HL7, DICOM, etc.), so that data can be interchanged between medical facilities, hospitals, etc.? If not, what does it exist?

Missing Answer (see the above)

- Do you agree reaching an agreement on the exact technical specs (both functional and non-functional) of the platform from the various user groups and project stakeholders, e.g., clinical doctors, lab doctors, consultants, nurses, technical personnel, etc.? If yes, how? if not, why?

Yes, of course we can reach an agreement. We would also need approval from Comunidad de Madrid (as they are responsible for HIS maintenance). The main issue in those projects is to ensure the security of the system, once this is solved (and there are different options) we are opened to implement it. For example, we are now designing a similar proposal for HIV patients connecting our system (laboratories, hospital pharmacy, etc. with an APP). This previous experience can help us with the next ones.

Barriers

- Reluctance or ignorance of the high management to support the project (with appropriate human resources and availability or working time)? Why?

The high management of the hospital is fully supportive with other telemonitoring projects.

- Reluctance of medical staff (doctors) to get involved in the project due to the lack of time (especially in the times of the pandemic) or not (please specify)?

I don´t think this will be an issue, personnel involved in this kind of projects are usually highly motivated. But one of the barriers that has been previously described is that clinical personnel don't confer the same level of confidence to information provided during in person visits than information collected through questionnaires and remote monitoring.

- Is there a lack of experienced technical personnel for both: (1) development & use of modern software tools (2) data processing skills combined with appropriate clinical knowledge (database management and data retrieval, data evaluation and cleansing, application of appropriate algorithms, evaluation of results, educated feedback and interpretation of results), or not (please specify)?

Our IT department has a high training both in technical aspects (development and use of modern software tools, data processing skills...) but they have also received a clinical training to ensure the communication with the clinical team. As I have previously mentioned, we are just involved in a similar project.

- In some cases, additional data are required from the patients, and the follow up of them is not so regular, so is it sometimes difficult to get in touch with them? How do you suggest solving it?

This can be an important issue. Previous studies have demonstrated:

The importance of the digital gap: selection of the right patients is important, and usability of the system is critical

Satisfaction surveys in this kind of projects have demonstrated patients are usually highly satisfied as they feel more in touch with their clinical teams. However, they need to be continuously engaged, they need to feel all this effort providing data is worth it and there is someone on the other side of their devices.

- Do you estimate any cost for the above?

It is difficult to estimate because it depends on many factors. I can say the cost form the HIV project I mentioned (design and implementation) is estimated in 180.000 euros.

Interview with Essen

Technical Requirements

- Is there availability of a complete and accurate Electronic Patient Record (EPR) and appropriate Information Systems to accommodate and support it (HIS, LIS, RIS/PACS)? If not, what is missing?

Yes, we have a complete EPR and HIS + LIS in our clinic. PACS is supported too and in daily use.

- Is there complete and accurate historical data in adequate depth of time? Please specify.

Yes, it's possible to provide the complete and accurate historical data in adequate depth of time.

- Can the RETENTION system be connected to the HIS/ERP or other hospital system?

Yes, the RETENTION system can be connected to the HIS/EPR at UK Essen.

- Is there a compliance with EPR standards (e.g., HL7, DICOM, etc), so that data can be interchanged between medical facilities, hospitals, etc.? If not, what does it exist?

Yes, the compliance with EPR standards is given.

- Do you agree reaching an agreement on the exact technical specs (both functional and non-functional) of the platform from the various user groups and project stakeholders, e.g., clinical doctors, lab doctors, consultants, nurses, technical personnel, etc.? If yes, how? if not, why?

Yes, we agree. It is necessary and purposeful to agree on the exact technical specifications as soon as possible in the next meeting.

Barriers

- Reluctance or ignorance or the high management to support the project (with appropriate human resources and availability or working time)? Why?

We do not foresee severe reluctance by IT department. Nevertheless, working time and resources needed for the project according to development, integration and interfacing of the RETENTION IT infrastructure must be defined as appropriate as possible.

- Reluctance of medical staff (doctors) to get involved in the project due to the lack of time (especially in the times of the pandemic) or not (please specify)?

We do not see a risk of reluctance by HCP involved in that project. However, the RETENTION infrastructure and app-design need to fulfil the need of easy to understand software so that patients feel comfortable in using the platform. Plus, we need to aim for a high level of automatism to allow for data inclusion by the HIS into RETENTION to avoid insertion of datasets by hand.

- Is there a lack of experienced technical personnel for both: (1) development & use of modern software tools (2) data processing skills combined with appropriate clinical knowledge (database management and data retrieval, data evaluation and cleansing, application of appropriate algorithms, evaluation of results, educated feedback and interpretation of results), or not (please specify)?

There is no lack of knowledge present at our institution. Again, the level of comfort in the application of RETENTION will be responsible for the success. Our IT department is keen is assisting and willing to integrate such platform.

- In some cases, additional data are required from the patients, and the follow up of them is not so regular, so is it sometimes difficult to get in touch with them? How do you suggest solving it?

Experience from previous and current studies conducted in our clinic has shown that close cooperation with the referring clinics leads to great success in these cases. Likewise, a good contact to the primary care physicians of the study patients is advantageous in order to obtain missing data. We believe our certified heart failure network (RUHR-HF) will help here, too.

- Do you estimate any cost for the above?

Without knowing all details according to the IT infrastructure and interface need, we are not able to foresee further costs at that point. However, we do expect further costs for IT personal staff. We will have to discuss here in person at our plenary meeting. There might be the opportunity to find synergism within all 5 clinical partners and the embedment of RETENTION in the present HIS and RIS software.

Interview with Bologna

Technical Requirements (5)

1. Is there availability of a complete and accurate Electronic Patient Record (EPR) and appropriate Information Systems to accommodate and support it (HIS, LS,BRIS/PACS)? If not, what is missing?

- Yes, we have availability of EPR

2. Is there complete and accurate historical data in adequate depth of time? Please specify.

- Yes, we have a complete set of historical data in clinical charts and on the hospital repository

3. Can the RETENTION system be connected to the HIS/ERP or other hospital system?

- No, it cannot because of internal firewalls and privacy management requirements.

4. Is there a compliance with EPR standards (e.g., HL7, DICOM, etc), so that data can be interchanged between medical facilities, hospitals, etc.? If not, what does it exist?

- Yes, data can be interchanged.

5. Do you agree reaching an agreement on the exact technical specs (both functional and non-functional) of the platform from the various user groups and project stakeholders, e.g., clinical doctors, lab doctors, consultants, nurses, technical personnel, etc.? If yes, how? if not, why?

- Yes.

Barriers (5)

1. Reluctance or ignorance or the high management to support the project (with appropriate human resources and availability or working time)? Why?

- There is no reluctance, albeit a bit of ignorance

2. Reluctance of medical staff (doctors) to get involved in the project due to the lack of time (especially in the times of the pandemic) or not (please specify)?

- No reluctance of medical staff

3. Is there a lack of experienced technical personnel for both: (1) development & use of modern software tools (2) data processing skills combined with appropriate clinical knowledge (database management and data retrieval, data evaluation and cleansing, application of appropriate algorithms, evaluation of results, educated feedback and interpretation of results), or not (please specify)?

- Personnel specifically dedicated to this aspect will be hired on Retention budget.

4. In some cases, additional data are required from the patients, and the follow up of them is not so regular, so is it sometimes difficult to get in touch with them? How do you suggest solving it?

- We do not have this issue, usually. We regularly follow up all our patients.

5. Do you estimate any cost for the above?

- The cost for the above has been factored as person/hour amount in the project budget**.**